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Using the 2018 Guidelines from the Joint Commission to Kickstart Your Hospital's Program to Reduce Opioid-Induced Ventilatory Impairment

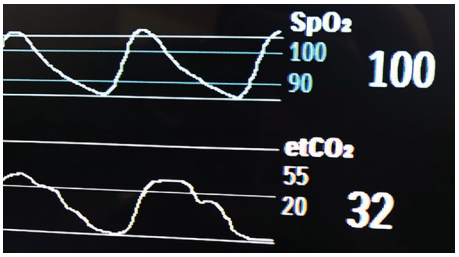
by Thomas W. Frederickson, MD, MBA, FACP, SFHM, and JE Lambrecht, MD, PharmD

In the hospital, opioids are the most commonly prescribed class of medications and the second most common class of medications associated with adverse events.[1,2] There are a range of adverse events associated with opioid use in the hospital. The most serious of these in terms of patient mortality is opioid-induced ventilatory impairment (OIVI). Approximately 1 in 200 hospitalized postoperative surgical patients suffer from OIVI.[3] One report identified 700 inpatient deaths in the U.S. directly attributed to patient-controlled analgesia between 2005 and 2009.[4] In addition to being common, and, at times, devastating to patients and caregivers alike, adverse events related to opioids are costly. In a 2011 study, annual costs in the U.S. associated with postoperative OIVI were approximately $2 billion.[5] The significant impact of OIVI on patient safety and health care costs has prompted many governmental and nongovernmental agencies to develop regulations and guidelines designed to reduce OIVI in the inpatient setting. One of the most recent and comprehensive of these guidelines is The Joint Commission R^3 Report issued in August 2017.[1]

The R^3 Report (R^3 stands for Rationale, Requirement, and Reference) provides standards for inpatient pain assessment and management designed to improve quality and safety. The standards focus on safe opioid prescribing and performance improvement, minimizing treatment risk, and performance monitoring and improvement using data analysis. This review will suggest four specific ways hospitals and their medical staff can implement some of these standards to decrease the risk of OIVI.

STRATEGY 1: ASSESSMENT AND MITIGATION OF PATIENT RISK FOR OIVI

When caring for postoperative patients and others receiving opioids in the hospital, clinicians must identify patients who are at high risk for developing OIVI. The history and physical exam is the mainstay for gathering important and specific knowledge about patients. Risk assessment and preoperative screening by the surgeon, anesthesia professional, hospitalist, and primary care physician are all helpful and can be used to gain insight for risk assessment. Comorbid conditions should be noted.



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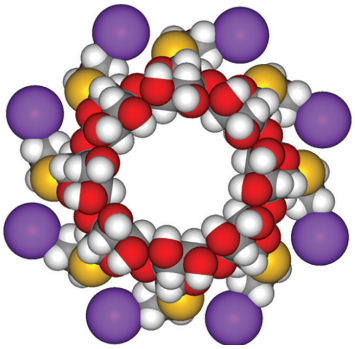
Current Status of Sugammadex Usage and the Occurrence of Sugammadex-Induced Anaphylaxis in Japan

by Tomoronori Takazawa, MD, PhD; Katsuyuki Miyasaka, MD, PhD; Tomorhiro Sawa, MD, PhD; Hiroki Iida, MD, PhD

Sugammadex is a synthetic cyclodextrin derivative that encapsulates aminosteroid muscle relaxants, especially rocuronium, to reverse their effect. Sugammadex (Bridion®, Merck Sharp & Dohme B.V., a subsidiary of Merck & Co., Inc.) was first released in the European Union in 2008 and then in Japan in April 2010. Sugammadex has been widely used since its release in Japan. Total sales of sugammadex in Japan reached $51,880,000 in 2010, more than four times that in Spain ($11,376,000), which was second in sales worldwide (data obtained from MSD K.K. (a subsidiary of Merck & Co., Inc.).[1] Sugammadex use in Japan has continued to grow with a total of 11,053,680 vials sold over the seven years since its release (© 2018 IQVIA/IMS-JPN (Japan) JPM (Japan Pharmaceutical Market), calculation based on JPM from April 2010 to June 2017 (reprinted with permission). It is not possible to accurately count the number of patients who have received sugammadex because multiple vials may be used on a single patient. Assuming that only one vial was used in most cases, sugammadex was administered to approximately 10% of the total Japanese population during the eight-year period since its release. Atvagoreverse® (a mixture of neostigmine and atropine) was used to reverse the effects of muscle relaxants in Japan before the release of sugammadex. The incidence of neostigmine is not exactly elucidated in the literature. However, there are only a few isolated case reports despite decades of its routine use to reverse neuromuscular blockade.



By Fvasconcellos (Own work) [Public domain], via Wikimedia Commons

Space-filling model of sugammadex sodium

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With this June *APSF Newsletter* issue, we are introducing our new APSF logo and branding. During the past few months, the Communications Committee has been working hard to bring a modern, energetic, new look to reflect our renewed commitment to Patient Safety in Anesthesia.

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APSF Newsletter Guide for Authors

The *APSF Newsletter* is the official journal of the Anesthesia Patient Safety Foundation. It is widely distributed to a variety of anesthesia professionals, perioperative providers, key industry representatives, and risk managers. It is published three times a year (February, June, and October). **Deadlines for each issue are as follows: 1) February Issue: November 15th, 2) June Issue: March 15th , 3) October Issue: July 15th.** The content of the newsletter typically focuses on anesthesia-related perioperative patient safety. Decisions regarding content and acceptance of submissions for publication are the responsibility of the editors. Some submissions may go in future issues, even if the deadline is met. At the discretion of the editors, submissions may be considered for publication on our APSF website and social media pages.

Types of articles include:

(1) **Review articles or invited pro-con debates** are original manuscripts. They should focus on patient safety issues and have appropriate referencing (see https://www.apsf.org/authors-guide.php). The articles should be limited to 2,000 words with no more than 25 references. Figures and/or tables are strongly encouraged.

(2) **Q&A articles** are anesthesia patient safety questions submitted by readers to knowledgeable experts or designated consultants to provide a response. The articles should be limited to 750 words.

(3) **Letters to the editor** are welcome and should be limited to 500 words. Please include references when appropriate.

(4) **Dear SIRS** is the "Safety Information Response System." The purpose of this column is to allow expeditious communication of technology-related safety concerns raised by our readers, with input and response from manufacturers and industry representatives. Dr. Jeffrey Feldman, current chair of the Committee on Technology, oversees the column and coordinates the readers' inquiries and the response from industry.

(5) **Invited conference reports** summarize clinically relevant anesthesia patient safety topics based on the respective conference discussion. Please limit the word count to less than 1000.

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The Official Journal of the Anesthesia Patient Safety Foundation

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Address all general, contributor, and subscription correspondence to:

Stacey Maxwell, Administrator
Anesthesia Patient Safety Foundation
Charlton 1-145
Mayo Clinic
200 1st Street SW
Rochester, MN 55905
Maxwell.Stacey@mayo.edu

Address *Newsletter* editorial comments, questions, letters, and suggestions to:

Steven B. Greenberg, MD
Editor-in-Chief, *APSF Newsletter*
greenberg@apsf.org

Edward A. Bittner, MD, PhD
Associate Editor, *APSF Newsletter*
bittner@apsf.org

Jennifer M. Banayan, MD
Assistant Editor, *APSF Newsletter*
banayan@apsf.org

Meghan Lane-Fall, MD
Assistant Editor, *APSF Newsletter*
lanefall@apsf.org

Send contributions to:

Anesthesia Patient Safety Foundation
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With Gratitude to Dr. John Eichhorn: *An Anesthesia Patient Safety Innovator*

by Mark A. Warner, MD

We extend our best wishes and gratitude to John H. Eichhorn, MD, as he transitions from over three decades of incomparable leadership and mentorship roles with APSF and within the specialty to finding more time to spend with his wonderful wife, Marsha, in retirement. Dr. Eichhorn was part of the original APSF leadership and was the founding editor of the *APSF Newsletter*. He led the *Newsletter* from its inception in 1985 until 2002 and continues to serve on its Editorial Board today. As APSF's archivist and in recognition of the foundation's 25th anniversary in 2010, Dr. Eichhorn created an extensive special *Newsletter* edition chronicling the remarkable positive influence that APSF has had on improving anesthesia patient safety. His contributions as *APSF Newsletter* founder, editor, and mentor to his successors have made the *Newsletter* the world's most widely distributed anesthesia publication.

Dr. Eichhorn, originally from Cleveland, Ohio, is a graduate of Princeton University and Harvard Medical School. After starting in general surgery, he switched to anesthesiology residency training at Harvard/Beth Israel Hospital in Boston. He joined the Harvard faculty in 1979 and remained there until moving to Jackson, Mississippi, in 1991 where he served more than a decade as professor and chair of anesthesiology at the University of Mississippi. He subsequently transitioned to the University of Kentucky, completing his distinguished career there and retiring in 2017.

Dr. Eichhorn's primary academic interests have been in the areas of anesthesia patient safety, standards of practice, risk management, and accident analysis. His landmark 1989 *Anesthesiology* paper was the first to suggest dramatic improvement in anesthesia patient safety through the behaviors of continuous intraoperative monitoring, best implemented by enhancing the human senses with early electronic warnings from capnography and pulse oximetry.[1] Dr. Eichhorn chaired the Harvard Anesthesia Risk Management Committee that wrote the original "Harvard standards" for intraoperative monitoring. These standards became the basis for many others, including those adopted by the American Society of Anesthesiologists and a great many other national societies around the world. Work from his International Task Force on Anesthesia Safety was the basis of the standards adopted by the World Federation of Societies of Anaesthesiologists. Dr. Eichhorn is especially proud of his contribution to the World Health Organization Surgical Safety Checklist. Also, his 1986 JAMA journal article describing the creation and adoption of the original monitoring standards[2] was honored in 2015 as number 10 in an historic compilation published in *Anesthesia and Analgesia* entitled, "Game changers: The 20 most important anesthesia articles ever published."[3]

There have been many awards and honors for Dr. Eichhorn in recognition of his contributions to improving patient safety. For example, in 2011 the Joint Commission/National Quality Forum consortium presented him with the highest honor in patient safety, the John M. Eisenberg Award for Individual Achievement in Patient Safety and Quality. Receiving a number of additional career recognition awards in the past decade, he continues to serve the specialty and our patients by tenaciously advocating for practice improvements that lead to better patient safety and outcomes.

John H. Eichhorn, MD

His time in APSF leadership roles is drawing to a close, but his efforts and their profound, positive impact will continue long into the future. Dr. Eichhorn has left a remarkable legacy and all of us and our patients are better for it.

Dr. Mark Warner is President of the APSF and the Annenberg Professor of Anesthesiology, Mayo Clinic, Rochester, MN.

Dr. Warner has no disclosures with regards to the content of the article.

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3. Barash P, Bieterman K, Hersey D: Game changers: the 20 most important anesthesia articles ever published. *Anesth Analg* 2015;120:663–670.

The APSF continues to accept and appreciate contributions.

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Planning Prevents Poor Performance: An Approach to Pediatric Airway Management

by Nicholas M. Dalesio, MD

Pediatric airway management remains a significant cause for perioperative morbidity and mortality. Emergencies arising from airway complications constitute 25 to 36% of all reported anesthesia closed-claims.[1-3] Of those, respiratory events are more common in children (43%) than in adults (30%), and children suffer a higher mortality rate (50% vs. 35%).[1-3] Furthermore, when the airway is difficult, practitioners require specialized skills.[4] Unlike in adults, the potential for a difficult airway in children can often be predicted, which provides an opportunity for preemptive planning. Thus, untimely deaths can be prevented through targeted development of anatomic knowledge, specific application of emerging technology, and advanced proficiency training and educational programs to broadly implement the specialized technique of pediatric critical airway management. At Johns Hopkins Hospital, we have created a multidisciplinary program to address pediatric airway management that includes 1) a Pediatric Difficult Airway Response Team (PDART), 2) a Pediatric Difficult Airway Consult Service (PDACS), and 3) a biannual multidisciplinary pediatric airway management educational course. Our primary goal is to create a service that will mitigate stress among providers, optimize patient safety, and eliminate morbidity associated with pediatric airway management.

Pediatric anatomy and physiology present unique challenges during airway management. A larger occiput in infants and young children (< 2–3 years of age) causes neck flexion in anesthetized children leading to airway obstruction.

Common Pediatric Anatomical Findings:

1) a cephalad trachea (the cricothyroid membrane is parallel to C4 compared to the C6 vertebrae in adults)
2) an omega-shaped, "floppy" epiglottis due to immature connective tissue at the vallecula
3) large tongue-to-mouth ratio
4) anteriorly angled vocal cords providing additional challenges for nonpediatric anesthesia professionals

Oxygen consumption is double that of an adult (6–7 ml/kg/min versus 3–4 ml/kg/min), and functional residual capacity (FRC) decreases substantially in the supine position, allowing cephalad movement of intra-abdominal contents that leads to rapid oxygen desaturation.[5] Additionally, hyper-responsive laryngeal reflexes, short vocal cord length, and subglottic narrowing may complicate endotracheal tube (ETT) placement. Infants and small children also have an overriding thyroid cartilage, making external airway anatomy indiscernible and surgical airway placement during an airway emergency extremely difficult.[6]

While several anatomical differences occur between the adult and child airway, some similarities in management occur. Adequate ventilation is paramount. Techniques to improve ventilation are similar to those in adults, including 1) two-handed mask techniques, 2) head tilt, 3) chin lift, 4) jaw thrust, 5) positive pressure, and 6) the use of oro- and nasopharyngeal airways when upper airway obstruction is suspected. Children's airways come in many more sizes than adults' airways,[7] necessitating accurate measurements of oro- and nasopharyngeal airways. The posterior aspect of the tongue can worsen obstruction with an oral airway that is too short, whereas an oral airway that is too long may push the epiglottis into the trachea, thus worsening airway obstruction.[8] Attention to ventilation pressures is also important. Aggressive mask ventilation can lead to gastric insufflation, further decreasing FRC and worsening hypoxia. The supraglottic airway (SGA; a laryngeal mask airway or LMA is a type of SGA) is another adjuvant that may improve ventilation. Many SGA subtypes are available and are differentiated based on their unique attributes including ease of use and ability to intubate through the internal lumen.[9]

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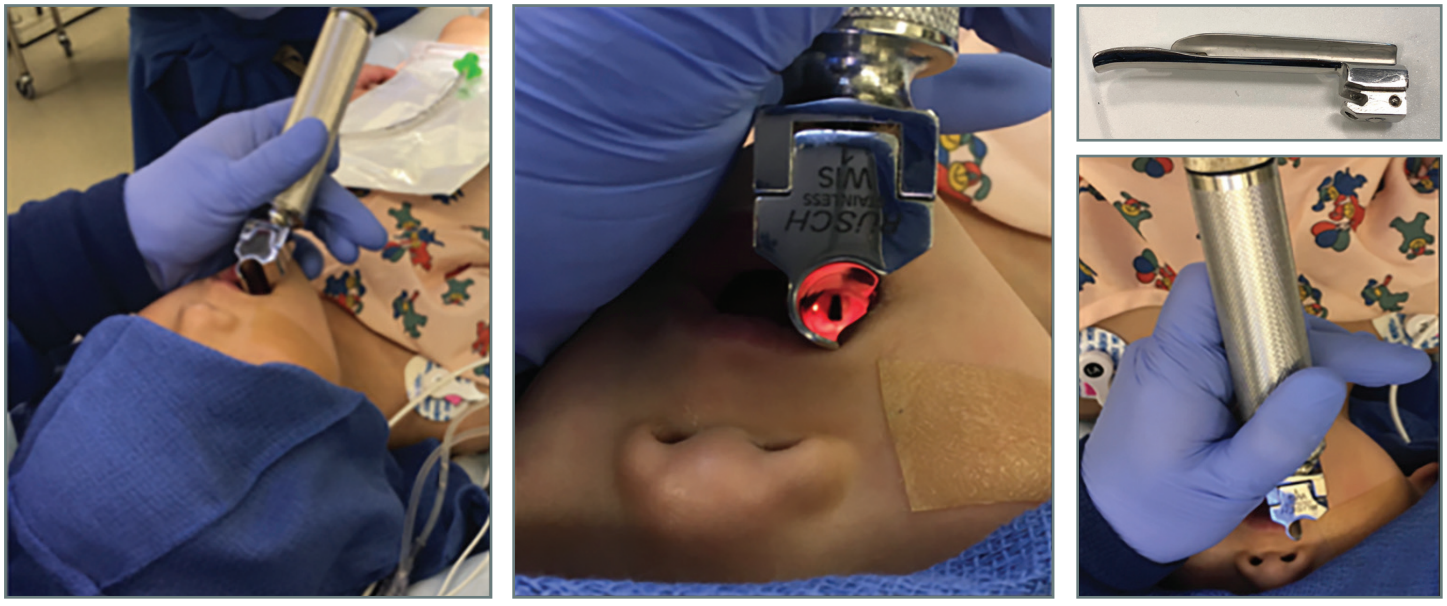

Figure 1: Retromolar intubation using a Wis-Hipple 1 laryngoscope. The blade is placed in the right retromolar space, bypassing the tongue, and advanced until the epiglottis can be displaced anteriorly to reveal the glottis.

Managing the Pediatric Difficult Airway

From "Pediatric Airway," Preceding Page

Several tools are used for tracheal intubation, with the primary technique being direct laryngoscopy. A variety of laryngoscope blades are available for pediatrics, but because of the anterior trachea and "floppy" epiglottis, many practitioners prefer using a straight (i.e., Miller) or semi-curved (Wis-Hipple) blade (Figure 1) for children under the age of 5 years.[10]

Pediatric difficult airway management can be divided into two categories: unanticipated and anticipated. Fortunately, the ***unanticipated*** difficult airway in "normal" pediatric patients is rare and often caused by trauma, infection, or inexperienced airway practitioners. Multiple intubation attempts by experienced pediatric anesthesia professionals defined as > 2 attempts, significantly increases complication rates. Alternative modes for securing the airway should be considered after two failed attempts by any practitioner.[11]

More commonly, the pediatric difficult airway can be ***anticipated.*** Alterations to airway anatomy from genetic, embryologic, or surgical causes can complicate pediatric airway management. Genetic and craniofacial syndromes that affect the airway are well described in the literature,[12] and plans can be formulated prior to induction of anesthesia. Knowing which device is optimal based on a patient's specific airway anomaly can help with appropriate preparation. An example of devices and techniques to consider when creating multiple airway contingency plans (described as plans A, B, and C) based on specific airway conditions are shown in Table 1. Patients with these conditions need to be identified early and before respiratory distress symptoms occur. It is our practice to develop and describe airway management plans within the medical record.[13] The pediatric anesthesia team is often best suited to initiate planning for and securing difficult airways should the need arise. If elective airway management is required for elective surgery, these patients should be cared for at a tertiary care facility, if possible.

Though many techniques and devices have been described for difficult airway management, there is a paucity of data showing superiority. In adults, the gold standard is an awake fiberoptic intubation (FOI); however, this procedure is often not possible to perform in small children due to poor cooperation.[14] Therefore, it is recommended that spontaneous ventilation be maintained during induction of anesthesia and intubation, using medications including inhalational anesthetics,[5] dexmedetomidine,[15] propofol,[16] and/or ketamine. Ensuring an adequate depth of anesthesia that prevents laryngospasm during airway manipulation while simultaneously maintaining spontaneous ventilation requires advanced skill and practice. Two common techniques to secure the airway include the use of videolaryngoscopes and FOI through a supraglottic airway (FOI-SGA). Videolaryngoscopy has been shown to improve the glottic visualization; however, the technique may increase the time to ETT insertion.[17,18] Using an SGA as a conduit can allow administration of inhalational anesthesia and continuous oxygenation and ventilation, avoiding hypoxemia in the most vulnerable pediatric population. A recent observational study published from data collected via the Multicenter Pediatric Difficult Intubation (PeDI) Registry reported that overall first-attempt success rates were similar for children with a difficult airway undergoing videolaryngoscopy and those undergoing FOI-SGA, even when controlling for patient factors such as anticipated difficult airway.[19] The caveat was that FOI-SGA had higher success rates with fewer incidents of hypoxia in children < 1 year of age, supporting the recommendation for continued oxygenation during intubation. A cuffed ETT should be used when securing a difficult airway in any patient, including children,[20] because it can compensate for an air leak without exposing patients to risks associated with re-intubation.

Pediatric difficult airway practice guidelines have been described,[13,21] primarily adapted from the adult difficult airway algorithm.[4] Alterations to the algorithm should focus on the unique attributes of the pediatric airway and physiology, replacing only the invasive airway management recommendations. For instance, maintaining spontaneous ventilation in children with an anticipated difficult airway is important. Infants and small children (~ < 20 kg) with high oxygen consumption and low FRC especially benefit from this type of management. Secondly, the term "multiple attempts" when describing failed intubation should be explicitly defined as more than two, and alternative approaches attempted thereafter. Institutions that care for children should have a variety of pediatric ETT sizes readily available and the value of a SGA use emphasized. Lastly, during an emergency when the "cannot ventilate, cannot intubate" scenario occurs, children under the age of 8 years should undergo needle cricothyrotomy as an invasive surgical technique. Surgical tracheostomies should not be performed in an emergency in this age group by non-surgical physicians.[22] Because the thyroid cartilage is overriding and the airway anatomy indiscernible via palpation, ultrasound guidance for needle cricothyrotomy should be considered, if available.[23]

Facilities that care for children should prepare for these emergencies with available rescue devices and should consider developing a multidisciplinary emergency airway response team.

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Table 1: Endotracheal intubation devices and techniques ranked for success within categories of airway pathology leading to difficult airway management.

	Upper Airway Obstruction			Craniofacial Abnormality		Neck Pathology	
Technique	Physical	Visual (blood)	Small Mouth Opening	Short TMD	Other	Soft Tissue (hygroma)	Cervical Spine Immobile
FOI-SGA	A	A	B	A	A	A	B
FOI alone	A	—	A	B	A	A	B
Retromolar	B	—	—	A	B	B	—
Videolaryngoscopy							
Glidescope®	C	B	C	A	B	B	A
C-MAC®	C	B	B	A	B	B	A
D-Blade* (adolescents)	C	B	C	B*	B	B	A
Elective Surgical Airway	C	C	C	C	C	—	—

*Table 1: Ranking of endotracheal intubation devices and techniques for difficult airway management in different airway pathologies. A = initial/best option; B = secondary option; C = last option; — indicates techniques unlikely to be successful or inappropriate for that airway pathology. TD, thyromental distance; FOI-SGA, fiberoptic intubation through supraglottic airway; FOI, fiberoptic intubation. *The D-blade has a sharp angled blade, decreasing the length from blade tip to handle. This device may be ideal for older children with large tongues and a short thyromental distance.*

Pediatric Airway Response Team May Aid Clinicians in Managing Difficult Airways

From "Pediatric Airway," Preceding Page

We developed a multicomponent Pediatric Difficult Airway Program at Johns Hopkins Hospital that consists of a pediatric airway management course, the PDART, and the PDACS. The program was created in collaboration with a multitude of pediatric specialists to improve safety and decrease morbidity, stress, and urgency associated with airway management in children.

MULTIDISCIPLINARY PEDIATRIC AIRWAY MANAGEMENT COURSE

The multidisciplinary pediatric airway course is designed to teach practitioners from all pediatric disciplines the basics of airway management, as well as advanced skills needed to manage different airway scenarios in infants and children. Since 2014, this biannual course has instructed residents and fellows, nurses, respiratory therapists, paramedics, and other clinicians who want to improve their pediatric airway management skills. After a few didactic lectures, participants practice using various ventilation and intubation devices via hands-on skill stations and engage in commonly encountered simulated scenarios. Pre- and post-learning is assessed through testing.

PEDIATRIC DIFFICULT AIRWAY RESPONSE TEAM (PDART)

The pediatric DART was adapted in November 2015 from the adult DART that originated at Johns Hopkins in 2008.[24] This multidisciplinary team, composed of pediatric anesthesiologists, otolaryngologists, trauma surgeons, respiratory therapists, nurses, and pharmacists responds to a call when initial responders require help with airway management or a child with a difficult airway requires airway management. Pediatric anesthesiology attendings facilitate the PDART by staying in-house 24 hours per day, 7 days per week. Emergency airway backpacks are stocked and carried to each PDART call by the pediatric anesthesiologist. The backpack houses laryngoscopes, SGAs, and materials for needle cricothyrotomy. If additional equipment is needed, such as a flexible bronchoscope, patients are mobilized (if possible) to the operating room. Videolaryngoscopes and flexible videobronchscopes are kept in one location for easy access within the operating room.

PEDIATRIC DIFFICULT AIRWAY CONSULT SERVICE (PDACS)

The PDACS was created to provide airway management plans before an at-risk patient develops respiratory distress. Consultation is made on either a routine or urgent basis. Routine consults are made for patients who have a history of difficult airway but are not experiencing any respiratory symptoms. If admitting physicians and/or nurses obtain information related to 1) difficult airway history or 2) any medical conditions that potentially alter the structure of the patient's face or airway, an electronic page goes to the pediatric anesthesiologist to complete the consultation. Urgent consultations are made if children with a history of or potential for difficult airway management shows signs of early respiratory distress, but immediate intervention is not needed. An urgent consult is made by a direct phone call to the pediatric anesthesiologist and completed within the hour. If the patient has a difficult airway, a consultation is complete when 1) a consult note is placed in the patient's chart, 2) "Difficult Airway" is added to the patient's Problem List, triggering a banner alert in the patient's medical record, 3) ventilation and intubation plans are

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2018 APSF Trainee Quality Improvement (TQI) Recognition Program

The project submission deadline for:

- **Resident Physician Anesthesiologists is August 31, 2018, at 11:59 pm**
- **Student Registered Nurse Anesthetists is July 15, 2018, at 11:59 pm**
- **Anesthesiologist Assistant Graduate Students is August 31, 2018, at 11:59 pm**

The APSF Committee on Education and Training announces the third annual and expanded APSF Trainee Quality Improvement Program. The 2018 program hosts tracks for resident physician anesthesiologists, student registered nurse anesthetists and anesthesiologist assistant graduate students. The APSF invites all US and Canadian anesthesia professionals in training to demonstrate their program's work in patient safety and QI initiatives. The top two projects in each track will receive APSF recognition and financial rewards of $1,000 and $500, respectively.

All submissions will consist of a video describing the QI project. All video abstract submissions will be created on a mobile device (example, iPhone or iPad).

The APSF will accept up to two completed submissions from each US and Canadian training program in each specialty track.

The submission process:

- Create a video showcasing your patient safety and quality improvement innovation
- Go online to www.dropbox.com and create an account
- Upload the video to the Dropbox account and share the file with the email address smarkan11@hotmail.com
- Send a brief email notification of your completed submission to the APSF Trainee QI Committee at residentqi@apsf.org. The committee will promptly review your material and acknowledge receipt.

Resident Physician and Anesthesiologist Assistant Graduate Students winners will be announced at the 2018 Annual Meeting of the American Society of Anesthesiologists and Student Registered Nurse Anesthetists winners will be announced at the 2018 Nurse Anesthesia Annual Congress. The winning entries will also be showcased on the APSF website. Please email any inquiries to residentqi@apsf.org. For more information please go to: Foundation—Announcements https://www.apsf.org/announcements.php?id=94

Expert Personnel and Specialty Equipment Aid in Securing the Pediatric Difficult Airway

From "Pediatric Airway," Preceding Page

summarized within the patient's Problem List and hand-written at the patient's bedside, 4) a "Difficult Airway" bracelet is placed on the patient, and 5) a "DART" identification card is placed on the patient's hospital room door.

CONCLUSION

Airway management in children, with an **unanticipated** difficult airway requires prior strategy implementation consisting of emergency response by expert personnel as well as specialty equipment including the SGA to be readily available. Children with an **anticipated** difficult airway should have structured airway management plans, labeled with appropriate alerts in the medical record, and undergo airway management by experts with extensive pediatric airway experience. Continuing education, including simulation of emergency situations, may help to maintain skills required for difficult airway management in children. More investigation is forthcoming as to whether the programs we and others have implemented reduce adverse events related to the pediatric airway.

Dr. Nicholas M Dalesio is an Assistant Professor of Anesthesiology at Johns Hopkins University Medical School and is in the Department of Anesthesiology/ Division of Pediatric Anesthesiology & Critical Care Medicine. Dr. Dalesio also has an appointment in the Department of Otolaryngology/Head & Neck Surgery practicing at the Johns Hopkins Bloomberg Children's Hospital, Baltimore, MD.

Dr. Nicholas Dalesio does not have any disclosures with regards to the content of the article.

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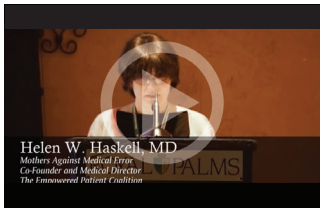

Opioid-Induced Ventilatory Impairment (OIVI): Time for a Change in the Monitoring Strategy for Postoperative PCA Patients (7 minutes)

Perioperative Visual Loss (POVL): Risk Factors and Evolving Management Strategies (10 minutes)

APSF Presents Simulated Informed Consent Scenarios for Patients at Risk for Perioperative Visual Loss from Ischemic Optic Neuropathy (18 minutes)

APSF Presents Prevention and Management of Operating Room Fires (18 minutes)

Joint Commission Emphasizes Pain Assessment and Monitoring Treatment Risk

From "Kickstart," Cover Page

Current use or previous exposure and response to opioids is also important to document, including a history of chronic opioid efficacy or tolerance, or of opioid-related adverse events. The history should also note chronic use of other sedative medications such as benzodiazepines and muscle relaxants. Risk also depends upon the type of surgery the patient will have and expected intensity and duration of postoperative pain.

Risk assessment is particularly difficult. Even though specific risk factors for OIVI are well described (Table 1), there is not a validated and comprehensive risk scoring system for OIVI in the perioperative setting. Adding to this complexity is that **every patient is at risk**. Patients who are opioid tolerant are at risk due to the potential difficulty with pain control and the need to escalate dosages. Opioid naïve patients are also at significant risk because of unpredictable responses to the initial dosages.

The Joint Commission Standards as outlined in the R[3] Report require that every patient's pain treatment is assessed and monitored in terms of both effectiveness and treatment risk. A team-based approach to risk assessment and mitigation should include roles for physicians, nurses and respiratory therapists, and could include alerts and risk scores for the most common and serious risk factors, including patients that are opioid naïve, those with renal failure, co-administration of other sedating medications, patient-controlled analgesia (PCA) use, the elderly, and the obese.

Figure 1: STOP-BANG[11]

1. **S**noring—Do you snore loudly?
2. **T**ired—Do you often have daytime tiredness, fatigue or sleepiness?
3. **O**bserved—Has anyone seen you stop breathing while you sleep?
4. Blood **P**ressure—Do you have or are you being treated for high blood pressure?
5. **B**MI >35 kg/m^2?
6. **A**ge >50 years?
7. **N**eck Circumference >40 cm
8. **G**ender—Male?

Answering YES to three or more of these eight questions puts the patient at HIGH risk for obstructive sleep apnea (OSA). If yes to less than three items then the patient is LOW risk.

[11] Adapted from: Chung F, Abdullah HR, Liao P. STOP-Bang Questionnaire: a practical approach to screen for obstructive sleep apnea. *Chest* 2016;149:631–8.

The Society of Hospital Medicine (SHM) currently has a mentored implementation program to institute hospital-wide risk reduction and patient safety improvement for patients receiving opioids (Reducing Adverse Drug Events due to Opioids or RADEO).[6] Experienced mentors are provided by SHM. These quality improvement and pain control experts help coach hospital-based teams to improve the quality and safety of opioid prescribing and administration at their hospitals. This study is evaluating a number of risk assessment strategies and risk mitigation approaches. Among these approaches are preoperative STOP-BANG (Figure 1) screening for obstructive sleep apnea with triage to postoperative continuous positive airway pressure or ventilation monitoring as appropriate. Electronic health record (EHR) alerts based on age and renal failure, and pharmacy screening for specific high-risk patients, medications, or medication combinations are also being evaluated.

At present, there is no single comprehensive strategy that can determine patient risk with OIVI with 100% accuracy. However, based on an analysis of challenges that your institution faces, our recommendation is that all hospitals have a risk assessment and mitigation strategy to decrease OIVI that is team-based, measured, monitored, and adjusted based on your outcomes.

STRATEGY 2: PRESCRIBING GUIDELINES AND STANDARDS

The Joint Commissions R[3] Report requires that hospitals have available non-pharmacologic pain treatment modalities and that pain treatment plans be based on the patient's history, clinical condition, and the goals of care. In addition, there are other elements that should be considered in developing prescribing practices within an institution.

We suggest the following:

1. Clearly **identify which clinical provider is responsible for pain management**, particularly postoperative pain. Agreement between specialties at a service line level needs to be in place and understood by the patient, nursing staff, and the pharmacy. The clinical provider responsible for pain management may differ based on location in the hospital—i.e., ED (ED physician), PACU (anesthesia professional), ICU (intensivist), and medical/surgical floor (hospitalist or surgeon).
2. **Standardized handoffs** should include all recent (within the last 4 hours, or 24 hours for long-acting or extended-release opioids) opioid dosage administrations.

Table 1: Risk Factors for Opioid-Induced Ventilatory Impairment (OIVI)

One or more of these risk factors indicate patients are at increased risk:

Age >55
Obesity (e.g., body mass index ≥ 30 kg/m^2)
Untreated obstructive sleep apnea
History of snoring or witnessed apneas
Excessive daytime sleepiness
Neck circumference ≥44.45 cm
Preexisting pulmonary or cardiac disease or dysfunction, e.g., chronic obstructive pulmonary disease, congestive heart failure
Smoker (>20 pack-years)
American Society of Anesthesiologists patient status classification 3-5
Concomitant administration of sedating agents, such as benzodiazepines or antihistamines
Continuous opioid infusion in opioid-naïve patients, e.g., IV PCA (Patient-Controlled Analgesia) with basal rate
First 24 hours of opioid therapy, e.g., first 24 hours after surgery is a high-risk period for surgical patients
Prolonged surgery (>2 hours)
Thoracic and other large incisions that may interfere with adequate ventilation
Large single bolus techniques
Naloxone administration: Patients given naloxone are at higher risk for additional episodes of respiratory depression

Increased opioid dose requirement:

Opioid-naïve patients receiving >10 mg of morphine or equivalent in post anesthesia care unit (PACU)
Opioid-tolerant patients who require a significant amount of opioid in addition to their usual daily dosing, e.g., the patient who takes an opioid analgesic before surgery for persistent pain and received several IV opioid bolus doses in the PACU followed by high-dose IV PCA postoperatively

Adapted from Pasero C, McCaffery M. Pain assessment and pharmacologic management. St. Louis: Mosby, 2011, p.516.

3. The use of **standardized order sets** that include nonpharmacological and multimodal approaches should be encouraged, or, ideally, required. This is especially important when using PCA. Order sets should comply with up-to-date prescribing safety standards and give clear prescribing instructions and parameters.

See "Kickstart," Next Page

Potential Components of a Pain Medication Prescribing Practice Program

From "Kickstart," Preceding Page

For example, the maximum dosage with a range should only be two times, and not more than four times the smallest dose, and orders should indicate whether the medication is to be used for mild, moderate, or severe pain. Intervals should be long enough to avoid "dose stacking." Pharmacists should review and approve all order sets.

4. Most hospitalized patients should have a **scheduled pain medication** if continuous pain is anticipated. Scheduled pain medications are also necessary for patients chronically receiving opioids to avoid opioid withdrawal. Scheduled pain medications can be non-opioid if the patient is not opioid-habituated.
5. Every patient with acute pain receiving opioid medications should have an **opioid de-escalation** strategy in place. Opioid de-escalation can be imbedded in order sets, based on policies and alerts that require daily re-ordering, or based on pharmacist review and recommendations. Opioid orders that are not time limited should be avoided altogether.

STRATEGY 3: PATIENT ASSESSMENT AND MONITORING STANDARDS

Much like risk assessment, there is a lack of clear evidence for optimal monitoring strategies of patients receiving opioids. The Joint Commission standards require the following.[1]

1. Provider access to state-run Prescription Drug Monitoring Programs (PDMPs) and Databases.
2. Access to monitoring devices such as pulse oximetry or capnography as deemed necessary by hospital admistration and medical staff jointly.
3. Hospitals have standards for screening, assessing, and reassessing pain that are appropriate for the patient's age, condition, and cognitive status.
4. Each patient's pain management plan is patient-centered, based on realistic and measurable expectations, based on treatment objectives, and is paired with patient and/or family education.

In addition, the Centers for Medicare & Medicaid Services (CMS) requires an assessment of risk for postoperative patients receiving IV opioids based on the frequency of dosing, mode of delivery, and duration of IV opioid therapy. In addition, hospitals must address what is to be monitored, how frequently (based on risk), progress towards goals, side effects, and adverse events.[7]

We recommend a number of best practices:

1. Seventy-five percent of the OIVI events occur within the first 24 hours after surgery.[8] Consequently, clinicians should especially focus on risk during this time period, including consideration of ventilation monitoring plus pulse oximetry for patients receiving opioids, especially those with, or at risk for, sleep-disordered breathing.
2. The APSF suggests using continuous monitoring of oxygenation and ventilation in patients receiving PCA or neuraxial opioids in the postoperative period.[9]
3. The ongoing assessment of pain should not solely be based on numeric (1–10) or subjective (mild, moderate, severe) scales. Pain assessments should include functional criteria that tie to the goals of care for the patient—for example, the ability to mobilize and the ability to sleep. Pain assessments should also be based on nursing judgment as well as patient input and goals of care.

Figure 2: Pasero Opioid-induced Sedation Scale (POSS)

S = Sleep, easy to arouse
Acceptable; no action required; may increase opioid dose as indicated.

1. Awake and alert
Acceptable; no action required; may increase opioid dose as indicated.

2. Slightly drowsy, easily aroused
Acceptable; no action required; may increase opioid dose if needed.

3. Frequently drowsy, arousable, drifts off to sleep during conversation
Unacceptable; monitor for respiratory depression and sedation level closely until sedation level is stable at less than 3 and respiratory status is adequate; decrease opioid dose 25% to 50% or notify prescriber or anesthesia professional for orders; consider administering a nonsedating, opioid-sparing nonopioid, such as acetaminophen or an NSAID, if not contraindicated.

4. Somnolent, minimal or no response to verbal or physical stimulation
Unacceptable; stop opioid; consider administering naloxone, notify prescriber or anesthesia professional; monitor for respiratory depression and sedation level closely until sedation level is stable at less than 3 and respiratory status is adequate.

Adapted from Pacero C. Acute pain service policy and procedure manual, Los Angeles: CA, Academy Medical Systems; 1994.

4. Every patient receiving opioids should have regular nursing assessments of the level of sedation at appropriate intervals including after dosing of an opioid. Level of sedation should be assessed approximately 15 minutes after dosage of IV opioids, and 30 minutes for PO administration. The most common sedation scale used to assess the sedating effects of opioids is the Pasero Opioid-induced Sedation Scale (POSS).[10] POSS is a part of the nursing flow sheet in most EHRs (Figure 2). The sedation scale, pain score, and nursing judgment and observation of functional assessment should be used by nursing to make decisions about administering PRN or scheduled opioids as well as other sedating medications.
5. Hospital providers who develop protocols that incorporate continuous monitoring with oximetry and capnography should recognize the benefits and limitations of these monitors and recognize the real dangers of alarm fatigue and the difficulty of setting alarm thresholds that are clinically meaningful.

STRATEGY 4: ENGAGING THE MEDICAL STAFF

Institutional support is critical to the success of any process or practice in your hospital, including implementing The Joint Commission's opioid safety standards. Support must occur at all levels. An executive sponsor for an "opioid safe practices committee" should help establish governance and develop a project charter that is aligned with the mission and vision of the hospital. In addition, the executive sponsor is essential in garnering necessary resources such as a project budget, purchasing capital, project management, dedicated clinician time, clerical support, and providing information technology (IT), data collection, and data analysis personnel.

Changes in clinical practice should be designed by front-line clinical staff and facilitated by medical staff leadership and administration. This is best achieved via a multidisciplinary committee involving physicians from different specialties, nursing, quality improvement staff, pharmacy, and IT personnel. In addition, The Joint Commission requires that the medical staff are involved in an ongoing quality improvement effort, including establishing metrics and analyzing data.

It is our opinion that a respected physician champion is critical for success. This physician can lead your committee and be the face of this effort to the medical staff.

See "Kickstart," Next Page

Key Elements in Developing an Opioid Safety Program

From "Kickstart," Preceding Page

An important role of this champion or other physician leaders is medical staff education which can occur via grand rounds or other methods that are effective in your hospital. Ideally this champion will also have the political savvy to help get support for needed changes.

Some further keys to engaging your medical staff are

1. Have a statement of purpose. It should be brief, coherent, and easily understood by interested parties. The statement of purpose explains why the opioid safety efforts are valuable to your hospital. An example of such a statement would be, "In 2019 and thereafter in our hospital we will have no serious adverse events related to opioids."
2. Recognize that not everyone will initially be on board with the opioid safety program. Anticipate concerns and provide answers. Help everyone see the value in this work. Tactics include both sharing data and patient safety stories. Get everyone to understand that their commitment really matters to patient care.
3. Identify key stakeholders and involve them early and gain their support. These are the individuals that will be needed in order to ensure the success of the project and also motivate and engage others. They will also provide valuable feedback and help formulate strategies for needed change.
4. Measure your baseline performance and set achievable and measurable objectives. Develop a scorecard to evaluate progress. Data should be transparent and reported broadly.
5. Develop a trusting environment. One key is not asking staff to increase their workload in order to participate on the project.
6. Focus on change management, keeping in mind that changes are easier when they are imbedded in existing clinical workflows. In addition, data collection can be taxing—when designing interventions that will be measured, keep in mind the time associated with data collection.

CONCLUSION

OIVI leading to respiratory failure and death is preventable. Opioid-related adverse events provide opportunities to reflect on current practices and institute systems and behavioral changes that will improve outcomes and produce safer patient care. The Joint Commission R^3 report and associated standards require all accredited hospitals to have a comprehensive opioid prescribing and administration safety plan. We recommend that hospital administration and medical staff leadership embrace these standards, not simply to be in compliance, but as an opportunity to improve the safety of opioid prescribing and administration within the hospital and reduce the risk of OIVI.

Dr. Frederickson is Medical Director of Hospital Medicine at CHI Health in Omaha, NE, and an Assistant Clinical Professor of Medicine at the Creighton University School of Medicine.

Dr. Lambrecht is an Assistant Professor of Medicine at the Creighton University School of Medicine and a staff hospitalist at CHI Health Creighton University Medical Center–Bergan Mercy.

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Incidence of Sugammadex Anaphylaxis May Be Similiar to Succinylcholine and Rocuronium

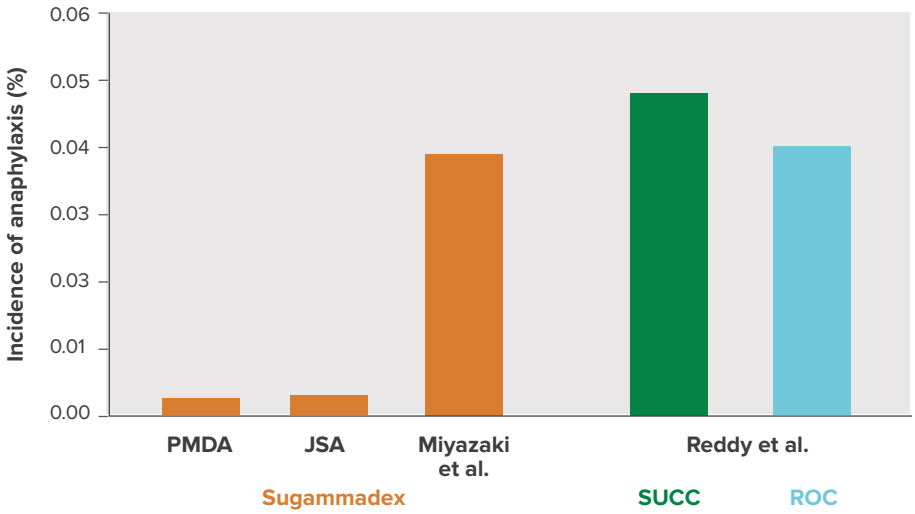
From "Sugammadex," Cover Page

While a dose of Atvagoreverse® (6 ml) costs about $6 US Dollars, a 200 mg dose of sugammadex costs about $90. Despite this enormous difference in price, sugammadex has rapidly become popular due to its reliability in reversing the effects of aminosteroid muscle relaxants. Other contributing factors for its wide use in Japan include unique features of Japan's nationwide health insurance system that substantially reduces the patient's financial burden and the aggressive promotion by the local pharmaceutical company. Consequently, many Japanese anesthesia professionals are unlikely to consider price when they select drugs to use during anesthesia.

There have been several reports on anaphylaxis caused by sugammadex in Japan.[1-4] According to the adverse events database of the Japanese Pharmaceuticals and Medical Devices Agency (PMDA—an agency similar to the Food and Drug Administration that handles pharmaceuticals and medical devices), 284 cases of sugammadex-induced anaphylaxis were reported between April 2010 and June 2017. Of these cases, 268 cases were reported by MSD, while the remaining 16 cases were reported directly by medical institutions. In accordance with government regulations, all the cases reported by MSD were critical, while the cases reported directly by medical institutions included noncritical cases. Of the total 284 cases, there were 157 cases reported as anaphylactic shock, 88 cases reported as an anaphylactic reaction, 4 cases reported as anaphylactoid shock, and 35 cases as an anaphylactoid reaction. The variety of names used to describe allergic reactions in the reports are likely due to variations in the definition of anaphylaxis in Japan. In the past, allergic events involving IgE were called anaphylaxis, while those not involving IgE were called anaphylactoid reactions. The use of the term "anaphylactoid reaction" is no longer recommended.[5] Based on the number of PMDA reported cases and total number of doses sold, the incidence of sugammadex-induced anaphylaxis is estimated to be approximately 1 in 40,000 cases (0.0025%).

According to data from the Japanese Society of Anesthesiologists (JSA) reported in June 2013 (based on reports from MSD), 95 cases of sugammadex-induced anaphylaxis (no mortality) occurred from April 2010 to October 2013.[6] Based on the number of patients who were estimated to have received sugammadex during the survey period (3.09 million patients), the incidence of sugammadex-induced anaphylaxis was calculated to be approximately 29 for every 1 million administrations (1:34,483, 0.0029%).[6] This estimate is close to the number obtained from the PMDA database (Figure 1). This similarity in the PMDA and JSA estimates is not unexpected since the data used were largely based on the same source, i.e., reports from MSD. However, it is unclear whether the incidence of sugammadex-induced anaphylaxis can be accurately estimated from these data because it is unlikely these reports capture all cases of anaphylaxis. In a recent Japanese single-center study, six cases of anaphylaxis were suspected to be caused by sugammadex during a three-year study period. This study estimated the incidence of sugammadex-induced anaphylaxis to be approximately 1 in 2,500 cases (0.039%) based on a study population of 15,479 patients.[7] The authors of this Japanese study referred to a previous observational study reported from two institutions in New Zealand, showing that the estimated incidence of anaphylaxis due to succinylcholine and rocuronium was 0.048% and 0.04%, respectively.[8] The authors of the former study concluded that the incidence of sugammadex-induced anaphylaxis is roughly equivalent to that of succinylcholine- and rocuronium-induced anaphylaxis (Figure 1).[7] It is important to note that the incidence of sugammadex-induced anaphylaxis was approximately 13 times higher than that reported by PMDA and JSA studies.

Figure 1: Comparison of the incidence of anaphylaxis to sugammadex, succinylcholine, and rocuronium.



PMDA: Pharmaceuticals and Medical Devices Agency
JSA: Japanese Society of Anesthesiologists
SUCC: succinylcholine
ROC: rocuronium

Of the 95 cases of anaphylaxis reported by the JSA, 76 cases clearly showed an onset time for sugammadex-induced anaphylaxis. The JSA study suggested that the onset of sugammadex-induced anaphylaxis occurred within five to ten minutes after administration in 50 (65.8%) and 66 (86.8%) cases, respectively, among a total of 76 cases of sugammadex-induced anaphylaxis, who had a confirmed onset time.[6] This is in contrast to a recent review of sugammadex-induced anaphylaxis which reported that the slowest onset was four minutes and the mean value was approximately two minutes after the administration of sugammadex.[9] Sugammadex is often administered after the end of surgery before extubation, but sugammadex-induced anaphylaxis may occur after extubation. Reported symptoms of sugammadex-induced anaphylaxis are commonly respiratory system-related, including edema of the airway and bronchospasm. Decreases in arterial oxygen saturation are reported in about half of the cases of sugammadex-induced anaphylaxis.[9] When severe respiratory symptoms appear after extubation, reintubation or other supportive treatment may be necessary. If the discovery of the symptoms is delayed, the patient's life may be at a severe risk. In facilities that transfer patients to the PACU, ICU, or other wards immediately after extubation, there may be a period when patients are not monitored closely, which could delay diagnosis and treatment.[6] Therefore, patients who are administered sugammadex should be observed carefully in the operating room for at least five minutes after administration. In addition, they should be monitored closely during transport.

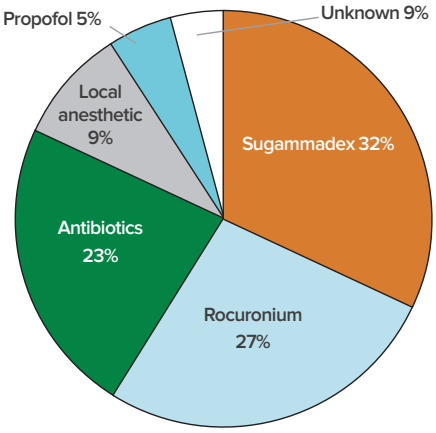
See "Sugammadex," Next Page

Sugammadex Anaphlyaxis May Occur Post-Extubation

From "Sugammadex," Preceding Page

A definitive diagnosis of anaphylaxis must satisfy the following conditions: presence of the clinical diagnostic criteria of anaphylaxis, high blood levels of histamine and/or tryptase, and a positive reaction to the culprit drug with skin testing.[10] The authors of this article performed skin tests on 22 patients with perioperative anaphylaxis at Gunma University Hospital and nearby medical institutions to determine the causative agents during the four years from May 2012 to March 2016. A causative agent for the perioperative anaphylaxis was identified in 20 out of 22 cases. The top three causative agents of perioperative anaphylaxis were sugammadex in eight patients (32%), rocuronium in six patients (27%), and antibiotics in five patients (23%) (Figure 2). The incidence of anaphylaxis due to each drug within our institutions is unknown because we did not track the total number of patients who received those drugs. However, it is true that sugammadex was the most common causative agent of perioperative anaphylaxis in our study. We presented these results at the 2016 63rd annual meeting of the JSA in Fukuoka, Japan. In a recently published study of potential sugammadex-induced anaphylaxis at a single center in Japan by Miyazaki et al., elevated plasma tryptase levels were observed in only one out of the six patients studied while the diagnosis of sugammadex-induced anaphylaxis was based on the timing of the appearance of clinical symptoms.[7] Although the skin testing is the gold standard for identifying the causative agent of anaphylaxis, it has some disadvantages. Skin testing may induce the recurrence of anaphylaxis, although the possibility is low. In addition, patients can experience pain during the skin testing. Specific IgE measurement is an alternative *in-vitro* method for allergy testing but requires a blood sample, and detection of sugammadex-specific IgE has not been reported. Recently, it has been suggested that the basophil activation test can be used for diagnosing sugammadex-induced anaphylaxis.[11] As with anaphylaxis caused by other drugs, performing multiple tests is necessary to increase accuracy in the diagnosis of sugammadex-induced anaphylaxis.

Figure 2: Drugs that cause anaphylaxis in the perioperative period.



The total percentage exceeds 100%, because a patient with multiple causative agents was included.

CONCLUSION

We have presented data that were reported by the PMDA, JSA, and data from Miyazaki et al., regarding the incidence of sugammadex-induced anaphylaxis. Given the variability in the reported incidences of sugammadex-induced anaphylaxis between studies, and the lack of a true denominator containing the number of sugammadex doses administered, a precise estimate of the incidence cannot be ascertained at this time. Since the reports by the PMDA and JSA used a framework in which physicians voluntarily reported cases of anaphylaxis, it is unlikely that these reports captured all cases of anaphylaxis resulting in underestimation. In contrast, the study by Miyazaki et al. is limited by small numbers, practice at a single institution, and insufficient testing. Although JSA annually asks member facilities to submit an incidence report of "accident cases" (cases where complications occurred but could not be forseen by anesthesia professionals), the primary objective of their report was not to estimate the incidence of anaphylaxis due to individual drugs. Thus, further studies are needed to determine the incidence of sugammadex-induced anaphylaxis in Japan and worldwide.

Sugammadex has rapidly gained popularity in Japan probably because many anesthesia professionals have been convinced of its effectiveness. However, in order to use sugammadex safely, anesthesia professionals should remain aware of the possibility of anaphylaxis and observe the patients diligently for at least five minutes after administration.

Dr. Takazawa is an Assistant Professor in the Intensive Care Unit at the Gunma University Hospital, Gunma, Japan.

Dr. Miyasaka is a Professor in the Department of Perianesthesia Nursing at the St. Luke's International University, Tokyo, Japan.

Dr. Sawa is a Professor in the Department of Anesthesia at the Teikyo University, Teikyo, Japan.

Dr. Iida is a Professor and Chair in the Department of Anesthesiology and Pain Medicine at the Gifu University Graduate School of Medicine, Gifu, Japan.

All authors are members of the Safety Committee of the Japanese Society of Anesthesiologists. The authors have no further disclosures as they pertain to the present article.

APSF EXECUTIVE COMMITTEE INVITES COLLABORATION

From time to time, the Anesthesia Patient Safety Foundation reconfirms its commitment to working with all who devote their energies to making anesthesia as safe as humanly possible. Thus, the Foundation invites collaboration from all who administer anesthesia, all who provide the settings in which anesthesia is practiced, and all individuals and organizations who, through their work, affect the safety of patients receiving anesthesia. The APSF is eager to listen to their suggestions and to work with them toward the common goal of safe anesthesia for every patient. If you are interested, please contact Mark Warner, MD at warner.mark@mayo.edu.

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EDITORIAL:

Sugammadex: The Anaphylactic Risk

by David Corda, MD, and Nikolaus Gravenstein, MD

New substances in our pharmaceutical armamentarium occur with reassuring frequency. When they tangibly affect our practice, they can be a tremendous clinical adjunct. While some do not withstand the test of time, others do. Sugammadex is an example of the latter. It gained FDA approval and arrived in the United States (12/2015) much later than in Europe (2008) or Japan (2010), where there are now many years of patient-accumulated experiences using this drug. In this *APSF Newsletter* issue, Dr. Takazawa and colleagues nicely detail the Japanese experience where it is estimated that up to 10% of the Japanese population has already been exposed to sugammadex.[1] With any drug, and especially a new one, there is always an underlying concern of a significant allergic reaction. In point of fact, the FDA delayed approval of sugammadex in the United States several times largely predicated on concerns surrounding hypersensitivity reactions.[2]

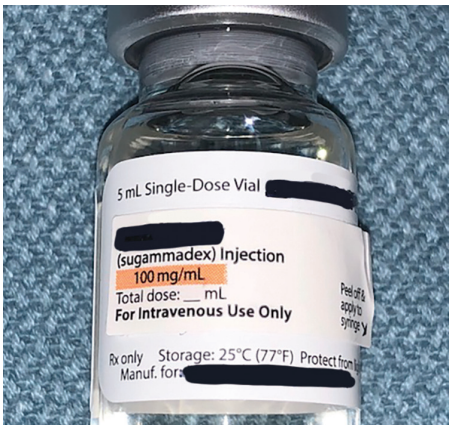
Although most sugammadex hypersensitivity reactions cause mild symptoms such as sneezing, nausea, rash, and urticaria, there is a small but finite risk of anaphylaxis with potentially life-threatening symptoms such as airway edema, bronchospasm, and cardiovascular collapse. Although the mechanism of sugammadex "anaphylaxis" remains unclear, it is encouraging that the risk does not seem to increase with repeated exposure, which is often inevitable with some patients. Interestingly, the risk of hypersensitivity reactions appears to increase with higher doses of the drug.[2]

As Dr. Takazawa et al. point out through their reported experience in Japan, the actual risk of sugammadex-induced anaphylaxis is very difficult to determine given the information to date. The authors report an incidence ranging from 0.0025% to 0.039%. This is a 15-fold difference depending on the use of data from the Japanese FDA equivalent or reporting from a single center study. As the authors suggest, much of this variability stems from difficulty in recognition, confirmation, and perhaps most importantly voluntary reporting. This voluntary reporting (numerator) that we also have in the United States makes it difficult to accurately estimate the incidence (the reported cases of anaphylaxis/total number of dose-exposed patients). So what do we know? The package insert from Merck and Co. describes an eyebrow-raising incidence of 0.3% hypersensitivity reactions in healthy study volunteers.[3] This is many-fold higher than the incidences described by Takazawa et al., and similarly far exceeds our own anecdotal two-year clinical experience. Ultimately, anaphylaxis is a binary event for the patient and the provider—either it happens or it doesn't.

So what lessons might we take from Takazawa et al. about this new drug and the concern for the possibility of an anaphylactic response? How is sugammadex anaphylaxis different from other anaphylactic reactions we see in the operating room? Historically, most intraoperative anaphylaxis is in response to the administration of an antibiotic, muscle relaxant, or latex—with the latter in decline as there is much less latex in modern operating rooms.[4] If one estimates the actual anaphylactic rate to sugammadex as roughly similar to that of rocuronium as referenced by Takazawa et al., then with the increased usage of sugammadex, we could estimate that the total incidence of intraoperative anaphylactic events will increase by at least one-third. If the current rate of intraoperative anaphylaxis is 1:10-20,000, it might increase to 1:6-14,000.[4]

With antibiotics, muscle relaxants, and latex, we expect and generally see reactions early in an OR case. Unlike these, sugammadex is typically administered at the end of a case. Thus a distinct difference is the timing of the anaphylaxis presentation and vigilance for anaphylaxis that may occur at what is historically an unexpected time for such an event. When sugammadex anaphylaxis happens, it seems to occur within 5 minutes of administration.[5] Interestingly, the likelihood of anaphylaxis with sugammadex appears to be dose-related.[3] Therefore, it would make sense to use the lowest effective dose to decrease the incidence of anaphylaxis. As an approximate rule of thumb, it requires 4 mg (3.57 mg to be exact) sugammadex to encapsulate/antagonize 1 mg rocuronium; thus a 200-mg reversal dose is adequate for most cases.[6]

Should significant anaphylaxis to sugammadex occur, the first-line treatment is small boluses of epinephrine titrated to response, followed by an epinephrine infusion when needed.[7] As an example, a case from our institution, which was reported to MedWatch, involved an elderly man with previous anaphylaxis to a non-steroidal anti-inflammatory drug. Rocuronium was reversed at the end of the case with 2 mg/kg sugammadex. One minute later, the patient's blood pressure dropped to a systolic blood pressure in the 40s with accompanied desaturation, skin flushing, and severe bronchospasm. The patient was treated with intravenous epinephrine (three 20-mcg boluses), diphenhydramine (50 mg), dexamethasone (12 mg) and famotidine (20 mg). The patient's symptoms subsided over 10 minutes, and he was briefly administered a low-dose epinephrine infusion. His tryptase level after the event came back significantly elevated at 74 ng/mL.[8] This was the first sugammadex anaphylaxis event in our institution after approximately 4,500 patients had been administered the drug. A second case approximately one year later presented as isolated bronchospasm without cardiovascular collapse and was resolved with two 20-mcg epinephrine boluses. It is encouraging that case reports and personal experience confirm that when sugammadex



anaphylaxis occurs, it responds to the usual therapy and that our anecdotal local incidence is < 1:4,000, i.e., < 0.025%.

In summary, anaphylaxis to sugammadex is a potentially high-consequence event that most assuredly happens as described by Takazawa et al. at some unclear but low frequency. It may occur without prior intravenous exposure. Importantly, anaphylaxis appears more likely at higher sugammadex doses, occurs at the end of case (within five minutes of exposure), and responds to standard epinephrine-based anaphylaxis treatment.

Dr. Corda is an Assistant Professor of Anesthesiology and Chief of Multispecialty Anesthesia at the University of Florida.

Dr. Gravenstein is The Jerome H. Modell Professor of Anesthesiology, Professor of Neurosurgery, and Professor of Periodontology at the University of Florida.

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Can Prescription Drug Monitoring Programs Aid Perioperative Clinicians in Reducing Opioid-Induced Ventilatory Impairment?

by David M. Dickerson, MD

More than 1.9 million Americans are estimated to have a prescription opioid use disorder.[1] A diagnosis of opioid use disorder is based on evidence of impaired control in avoiding use, social impairment, risky use, spending a significant time obtaining and using opioids, diminishing returns or tolerance to opioids and withdrawal symptoms that occur after stopping or reducing use.[1] Treatment for opioid use disorder with bupenorphine therapy increased by 52% from 2012 to 2016.[2] The misuse of opioids contributes to tens of thousands of deaths each year; in 2016 overdose deaths associated with opioids surpassed death from motor vehicle crashes.[1,3] In the February 2018 issue of the *APSF Newsletter*, patient- and practice-based risk factors for opioid-induced ventilatory impairment (OIVI) were discussed.[4] Identifying patient risk factors can be challenging, but there is a tool available to help anesthesia professionals and other perioperative clinicians identify patients with prior and current opioid use—prescription drug monitoring programs (PDMPs). This article reviews the relationship of prior opioid use to OIVI (including the concept of differential tolerance) and discusses how perioperative clinicians may utilize PDMPs to better identify patients in whom opioid tolerance may contribute to risk for OIVI.

Table 1: Factors* included in Risk Index for Overdose or Serious Opioid-Induced Respiratory Depression (RIOSORD)[15]

Has the patient received care for any of the following health conditions in the past 6 months?

- Substance use disorder (abuse or dependence) (includes alcohol, cannabis, cocaine, hallucinogens, opioids, and sedatives/anxiolytics
- Bipolar disorder or schizophrenia
- Stroke or other cerebrovascular disease
- Kidney disease with clinically significant renal impairment
- Heart failure
- Nonmalignant pancreatic disease
- Chronic pulmonary disease
- Recurrent headache

Does the patient consume any of the following?

- Fentanyl†
- Morphine†
- Methadone†
- Hydromorphone†
- Extended release or long-acting formulation of any prescription opioid†
- A benzodiazepine†
- An antidepressant

Does the patient currently consume a prescribed opioid dose greater than or equal to 100 mg morphine equivalents per day on a regular basis?†

*Each factor is associated with a different number of points or risk contribution in the RIOSORD.

†Reported in prescription drug monitoring programs.

RIOSORD was validated in both Veterans Health Administration (VHA)[14] and non-VHA[15] populations. This table uses risk factors from the non-VHA validation study.

NATIONAL TRENDS IN OPIOID PRESCRIPTION AND OPIOID ABUSE

The acute rise in medical opioid prescriptions over the past two decades has driven an increasing prevalence of potentially opioid-tolerant and opioid-dependent individuals presenting for procedural care.[3,5] Over the past ten years, there are mixed data regarding trends in prescription opioid use. National opioid prescription rates peaked in 2012, and there has been a slight decrease in the number of prescriptions and prescribed dosages since then. However, data show that prescribed duration of therapy slightly increased from 2006 to 2016; the percentage of opioid prescriptions for a greater than 30-day supply increased from 17.6% to 27.3% from 2006 to 2016.[5] From 2013 to the present, the percentage of prescriptions for >30-day supply has decreased slightly, but not enough to offset the net 9% increase since 2006.[5]

PREVALENCE OF PREOPERATIVE OPIOID USE

Rates of preoperative opioid use vary across surgical populations and are higher than in the general public. In Canada, 18.5% of patients presenting for ambulatory surgery were taking opioids preoperatively.[6] A U.S. study of patients undergoing spinal fusion had significant variability in the use of preoperative chronic opioid therapy, with the majority (71.7%, 1,787/2,491) using some preoperative opioids (58.5% with long-term, 24.5% with episodic use, 5.3% with short-term use).[7] These studies suggest geographic and procedure-related variation as well as methodological variation in defining chronic exposure.[7,8]

PERIOPERATIVE MANAGEMENT OF THE OPIOID-TOLERANT PATIENT

Preoperative opioid use and pain create significant challenges for the perioperative clinician. Preoperative opioid use predicts uncontrolled pain, increased costs, and poor satisfaction after orthopedic and general surgery.[9-12] Retrospective studies suggest a correlation between chronic or preexisting opioid use with an increased likelihood of in-hospital respiratory depression requiring intervention and subsequent catastrophic injury.[13] Research validating the Risk Index for Overdose or Serious Opioid-Induced Respiratory Depression (RIOSORD) suggests that opioid-tolerant patients are at significant risk for OIVI relative to patients without a history of opioid prescriptions and/or opioid tolerance.[14,15] For example, a patient taking short-acting morphine in excess of 100-mg morphine equivalents per day would score 18 points on the 146-point RIOSORD scale, corresponding to a 29.8% probability of OIVI. If that same patient were to also have a substance use disorder (abuse or dependence), this risk jumps to 83.4%.[15] Table 1 details the patient factors that contribute to the RIOSORD. Over the past decade, treatment for opioid misuse has increased, as have opioid prescribing rates.[5] Given the risk for OIVI in this population, heightened provider awareness is paramount.

RELEVANCE OF PREOPERATIVE OPIOID USE TO OIVI

A recent review estimates that the incidence of postoperative OIVI is approximately 0.5%.[16] In one study included in this review, opioid dependence or abuse contributes to OIVI with an odds ratio of 3.1 (95% CI:2.7-3.6), and previous substance abuse and chronic pain strongly predict opioid overdose.[17,18] Preadmission substance abuse history, opioid exposure, and benzodiazepine exposure are major predictors in the aforementioned RIOSORD.[14,15] While these retrospective studies are compelling, prospective studies are still needed to adequately characterize risk factors for OIVI.

DIFFERENTIAL TOLERANCE: A POTENTIAL MECHANISM FOR OIVI IN THIS POPULATION

It may be counterintuitive that opioid tolerance is associated with a higher risk of OIVI. However, tolerance of opioid-induced analgesia does not correlate with tolerance to OIVI.[19,20] This may be related, in partto the finding that opioid-dependent patients may exhibit impaired hypercapnic ventilatory response even in the absence of acute opioid exposure.[21] Continued opioid administration or dose escalation potentiates opioid-induced respiratory depression and sedation and may reflect differential tolerance.[16] In closed-claims analysis, sedation was identified as a preceding symptom of OIVI in 62% of the events.[4] Animal studies demonstrate differential tolerance develops within a matter of hours of initial opioid exposure suggesting a potential issue for opioid-naïve individuals.[22]

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Prescription Drug Monitoring Programs May Help Guide Clinicians in Developing a Perioperative Pain Care Plan

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Lee et al. discuss the potential challenges of implementing a comprehensive OIVI risk factor checklist.[4] Still, a standardized approach for identifying key patient factors, such as preoperative opioid use, may be useful in developing analgesic strategies that account for differential risk of OIVI. One such approach is PDMPs, which may aid clinicians in identifying those patients who either have previously used or are actively using opioids or benzodiazepines (another RIOSORD risk factor[14]), and who may be subsequently at higher risk for perioperative OIVI.

PRESCRIPTION DRUG MONITORING PROGRAMS (PDMPS)

PDMPs are state-administered monitoring programs that detail pharmacy-dispensed controlled substances shortly after the medication is released to the patient. Currently enacted in all 50 states, PDMPs (also called prescription monitoring programs—PMPs) provide a mechanism for identifying preoperative opioid and benzodiazepine use. Aberrant behaviors such as frequent opioid prescriptions from multiple prescribers suggest prescription misuse or overuse, and these patterns would be identifiable from PDMP records. Methadone dispensed by methadone clinics represents a blind spot, as it does not typically appear in PDMPs, but several states have proposed such inclusion to their state legislatures. Another reported pending addition to state-run PDMPs is the inclusion of Emergency Medical Services administration of naloxone.

Despite being run by states, there is a mechanism for sharing information across PDMPs. The PMP InterConnect® program of the National Association of Boards of Pharmacy (NABP) enables the 45 enrolled states to view prescribing data of the other NABP participant states.[23] This InterConnect® system may allow for regulatory bodies and clinicians to identify those patients seeking care from multiple providers in states with separate PDMPs.

THE IMPACT OF PDMPS ON OPIOID PRESCRIBING

PDMPs may reduce opioid overdose deaths and curb opioid prescribing rates via heightened clinician awareness of high-risk use including misuse or diversion. For instance, Florida saw a 25% reduction in oxycodone-caused mortality after PDMP implementation and other states have seen similar trends.[24] Registration and use mandates as well as use exemptions are state-specific. Mandating health care professionals register for PDMP use significantly reduced opioid prescribing rates in adopting states, yet mandating clinicians use the PDMP for specific care scenarios did not create incremental reduction when combined with registration mandates or implemented independently.[25] This suggests provider awareness of PDMPs via registration enables appropriate prescribing and suggests that use mandates may have too narrow of a scope to impact measurable changes in prescribing data.[25]

The clinical utility and impact of PDMP review by perioperative clinicians, however, is unknown and is a topic for future study. High-value utilization requires awareness of the PDMPs existence and capabilities, the current national trends in opioid use and misuse, and the clinical relevance of ongoing opioid use and addiction as factors in perioperative outcomes.

THE PDMP: A VALUABLE TOOL FOR PERIOPERATIVE CARE?

When the state of Illinois amended its controlled substance act requiring all clinicians to register to use the PDMP, relevance for many anesthesia professionals and intensivists was unclear, because both groups rarely prescribe post-hospital opioids. However, there are several reasons that PDMPs may be useful to perioperative clinicians.

First, PDMPs can be used to evaluate a patient's preoperative or preadmission opioid exposure and potential for tolerance, misuse, or dependence. Preoperative clinics could use the PDMP to identify and guide candidates for preoperative opioid weaning or increased monitoring on the day of surgery. PDMPs also facilitate gathering information that may be unobtainable due to the emergent or urgent nature of presentation, as in a trauma setting.

Second, they may help in the creation of analgesic regimens for opioid-tolerant patients, who are at risk for severe, uncontrolled, and persistent pain. While recommended by multisociety postoperative pain guidelines, comprehensive preoperative evaluation of patient's pain or psychiatric history varies substantially in practice,[26] and PDMP review could constitute part of this history taking. Recognizing a pattern of frequent prescriptions from multiple providers or longstanding benzodiazepine prescriptions may suggest potential complexity in pain management,[11,15,18] and might inform clinicians about the appropriate analgesic choices or the decision to obtain an early acute pain service consultation. Additionally, patients may not always be forthcoming due to fear of stigma, fear of legal consequences, or other concerns. PDMPs, while not comprehensive, provide information that may not be disclosed.

Third, discussion with patients of prescription data found in the PDMP may identify potential discrepancies or instances in which patients filled but did not take a prescription. Such instances can provide valuable and relevant information such as potential side effects, intolerance, or inefficacy when exposed to that medication previously reflecting occult pharmacogenomic issues or potential safety issues.

Finally, partial opioid receptor agonist/antagonists such as buprenorphine also appear in the PDMP. Identifying use of these agents facilitates broadened treatment planning and possible case deferral for possible cessation of such therapy prior to more painful surgery. Importantly, the presence of such medication suggests potential ongoing medication-assisted treatment for addiction, a comorbidity known to increase the risk of in-hospital respiratory failure.[14]

While far from a standard of care, the supplementary information offered by PDMPs may improve the quality of care provided to patients with preoperative opioid use, tolerance, or misuse. Moving forward, integration of PDMP data into electronic health records in a dynamic fashion (as opposed to the "flat" or read-only formatting most in use today) will enable the use of clinical decision support tools that may help in further mitigating risk of OIVI and improve analgesia for opioid-tolerant patients.

CONCLUSION

Prescription drug monitoring programs may offer a novel, supplementary data source for gathering important patient information for perioperative treatment planning and risk stratification. The multidisciplinary discussion of PDMP data preoperatively can guide preoperative patient preparation and education, perioperative pain care, postoperative and postdischarge monitoring and patient follow-up. The value of such utilization relies on provider recognition of the prevalence and significance of preoperative opioid use and misuse and the specific relationship between these factors and perioperative outcomes.

Dr. Dickerson is Director of the Acute Pain Service and Assistant Professor in the Department of Anesthesia & Critical Care at the University of Chicago.

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Marjorie Stiegler, MD, APSF Director of Digital Strategy and Social Media

The APSF is eager to connect with patient safety enthusiasts across the internet on our social media platforms. Over the past year, we have made a concerted effort to grow our audience and identify the best content for our community. Starting from scratch, we've seen increases in followers and engagement by several thousand percent, and we hope to see that trajectory continue into 2018. Please follow us on Facebook at www.facebook.com/APSForg and on Twitter at www.twitter.com/APSForg. Also, connect with us on Linked In at www.linkedin.com/company/anesthesia-patient-safety-foundation-apsf. We want to hear from you, so please tag us to share your patient safety related work, including your academic articles and presentations. We'll share those highlights with our community. If you are interested in joining our efforts to amplify the reach of APSF across the internet by becoming an Ambassador, please reach out via email to Marjorie Stiegler, MD, our Director of Digital Strategy and Social Media at Stiegler@apsf.org or to Emily Methangkool, MD, the APSF Ambassador Program Director at Methankgool@apsf.org. *We look forward to seeing you online!*

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Safe Gas Systems and Office-Based Anesthesia

by Jonathan L. Wong, DMD, and Gerhard Gschwandtner, PEng

CURRENT TRENDS IN OUTPATIENT ANESTHESIA

Outpatient sedation and anesthesia is nothing new. Ambulatory surgical centers are commonplace and widely accepted as a safe, convenient, and cost-effective means of delivering surgical care. Off-site anesthesia in locations remote to the operating room is also becoming increasingly prevalent. Office-based anesthesia (Figure 1) qualifies as a remote location and continues to grow in obstetrics and gynecology, plastic surgery, fertility clinics, ophthalmology, gastroenterology, and dentistry.

Dentists pioneered many of the techniques of anesthesia in an outpatient setting and were at the forefront of office-based anesthesia as well. So why are dental offices under such criticism? One major reason is that many dentists and oral surgeons continue to practice as operator anesthetists without adequate training of their support personnel and a lack of appropriate equipment. This was the basis of the unfortunate circumstances in California that led to the proposal of Caleb's Law after six-year-old Caleb Sears died during anesthesia administered by his oral surgeon. However, several of the recent public tragedies in dental offices have involved separate anesthesia professionals. These clinicians include physician anesthesiologists, certified registered nurse anesthetists (CRNAs), and dentist anesthesiologists. One of the possible causes of morbidity and mortality is the lack of safety checks in dental offices. One such safety check that is almost entirely overlooked is that of the medical gas system.

Figure 2: Zone Valve Box: A – 3 piece full port shut-off valve, B – Zone Valve Assembly label, C – Patient side vacuum/pressure indicator gauge.

Figure 1: Outpatient office where anesthesia can be delivered.

NFPA AND NFPA 99

The National Fire Protection Association (NFPA) is a global nonprofit organization, established in 1896, devoted to eliminating death, injury, and property and economic loss due to fire, electrical, and related hazards. It is widely known as a codes and standards organization that continually updates codes on a three- to five-year cycle in a process that is open and consensus-based. Technical committee members are typically volunteers. As Mr. Rusty Chase, a fire marshal, certified fire inspector, and paramedic, stated, "Many code items are developed to address issues that have severely injured or killed people in the past (personal communication)."

NFPA 99 is the Healthcare Facilities Code. It is updated every three years. NFPA 99 is the national code (American National Standards Institute or ANSI) for *all medical and dental gas installations* in the United States. It is also adopted by reference in the International Plumbing Code and International Fire Code, which are the basis for a majority of state and local building codes (these vary by locality).

Many anesthesiologists, nurse anesthetists, oral and maxillofacial surgeons, and dentists mistakenly believe that the NFPA 99 is merely about fire safety. This is a misconception. NFPA is actually about patient safety and prevention of medical gas mistakes.

See "Safe Gas Systems," Next Page

Dental Offices Are Not Exempt From Following NFPA 99

From "Safe Gas Systems," Preceding Page

NFPA 99 contains the minimum requirements for piped gas systems, equipment, materials, alarms, installations, testing, verification, and maintenance. The requirement applies to all health care facilities in the U.S., including hospitals, outpatient facilities, clinics, medical offices, and dental offices. Since at least 1996, NFPA code has required dental offices providing sedation and anesthesia to be compliant with these minimum standards.

NFPA 99 defines 3 categories (previously called levels) of medical and dental gas systems (Table 1). These categories define the specific minimum requirements for each system. The assessment of which category a facility or dental office falls under is based on a risk assessment and not by facility type or occupancy permit. NFPA has assigned certain depths of anesthesia and sedation to each of its three categories. The NFPA adopts the definitions of minimal, moderate, and deep sedation and general anesthesia from the American Society of Anesthesiologists' "Continuum of Depth of Sedation" Guideline.[1] In addition, the above definitions were reiterated and both minimal and moderate sedation further described in the latest Practice Guidelines for Moderate Procedural Sedation and Analgesia.[2]

These designations also do not change even if such services are only offered on a nonroutine basis. The designations do not change even if fewer than four individuals could be incapacitated at the same time. There is a popular misconception that dental offices do not need to comply with NFPA 99. This misconception may stem from the NFPA 101 Life Safety Code, which relates to occupancy and applies when four or more individuals could be incapacitated (under or recovering from sedation/anesthesia) at the same time; an office is not exempt from following the NFPA 99 guidelines.

ANESTHESIA PROFESSIONALS AND MEDICAL GAS SYSTEMS

Anesthesia professionals are primarily trained in the operating room. Training also occurs in hospitals and ambulatory surgery centers. These facilities, even at remote sites, must comply with NFPA 99 standards. As professionals, we are not trained to deal with the technicalities of these medical gas systems. The authority having jurisdiction (AHJ) is often the fire marshal who is not always aware of the level of anesthesia to be provided in an office. This is especially true of dental offices, in which it is often assumed that the office will be using just nitrous oxide and a dental air system (Category 3). Compounding this problem is the fact that anesthesia professionals may mistakenly assume that dental (Category 3) systems are the same as other medical gas systems that are familiar to them. This is, in part, due to the fact that Category 3 systems are not routinely discussed in texts or training programs,[3] as these nitrous dental gas systems were not intended for sedation and/or general anesthesia. Both dental and medical gas systems must be installed by an American Society of Sanitary Engineers (ASSE) 6010 Certified Medical Gas Installer, as there are strict rules for brazing and testing these piped systems. Plumbers that are not certified medical gas installers mistakenly install some of these systems. This has resulted in medical gas line cross-overs that have resulted in several deaths in dental offices due to hypoxic gas mixtures being delivered to patients. For this reason, all systems except dental Category 3 systems, even when installed by an ASSE 6010 Certified Medical Gas Installer, must then also be independently tested and verified by an ASSE 6030 Medical Gas Verifier (who has an additional two years of training with an associated certification when compared to the ASSE 6010) prior to use.

Additional patient and staff safety concerns arise from the dental air compressors and dental vacuum systems. Dental air compressors are designed simply for driving dental surgical instruments. It is highly unlikely that these systems could be mistaken for medical air, and thus will not be discussed further. However, dental vacuum pumps are designed to operate "wet" and do not have a collection canister to prevent contamination of the vacuum line. Instead, dental suctions have a "trap" built into the dental delivery unit to prevent large debris from entering the "wet" system. In the event of regurgitation, this system clogs with debris and will immediately fail. These vacuum pumps are designed to operate at high flow but low vacuum. For example, most dental vacuums operate at 10-13 inches of mercury, whereas a medical vacuum is required to maintain a minimum of 19 inches of mercury.

See "Safe Gas Systems," Next Page

Table 1: NFPA 99 Categories of Medical/Dental Gas Systems

NFPA 99 2018 Edition			
Category Type	**Category 3**	**Category 2**	**Category 1**
Permissable Depth of Anesthesia[a]	Nitrous anxiolysis and minimal sedation	Moderate sedation	Deep sedation and general anesthesia
Zone Valves[b] **Required**	No	Yes	Yes
Zone Alarms Required	No	Yes	Yes
Master Alarm Panel	Yes[c]	Single	Dual[d]
Controls for Line Pressure	Per manufacturer	Maintain stable pressure and flow for peak demand	Maintain stable pressure and flow for peak demand
Vacuum System	Dental vacuum	Simplex[e]	Duplex,[d,e] separate from dental vacuum
Waste Anesthetic Gas Scavenging	None	Nitrous scavenging may run through dental vacuum system	Separate Waste Anesthesitic Gas Disposal (WAGD) and medical vacuum from dental vacuum
Testing and Verification	In dental offices using dental gas systems, follow local code and manufacturer specs	American Society of Sanitary Engineers (ASSE) 6030 3rd Party Verifier	American Society of Sanitary Engineers (ASSE) 6030 3rd Party Verifier
Installation	Brazed, soldered, or fitted joints	Brazed with nitrogen purge	Brazed with nitrogen purge
Reserve Gas Supply	Minimum not required	One-day reserve supply	One-day reserve supply

[a] NFPA adopts the definitions for sedation and anesthesia from the American Society of Anesthesiologists' "Continuum of Depth of Sedation" verbatim

[b] Zone Valves are mechanical shut offs for medical gas and vacuum supply lines to each anesthetizing location and each supplied zone such as the PACU. Per NFPA, pressures must be monitored downstream of the valve for each gas and upstream for each vacuum supply line **(Figure 2)**.

[c] Limited, need not provide real time pressures, only low supply pressure

[d] 2018 NFPA 99 Chapter 15 allows a simplex system in a dental office

[e] Simplex refers to a vacuum system that may have multiple vacuum sources, but cannot generate 100% of the demand independently, and therefore is not redundant. A duplex system has 100% redundancy and can operate at capacity with a single source failure.

Routine Maintenance/Certification of Office-Based Gas Systems is Recommended

From "Safe Gas Systems," Preceding Page

The variability in fresh gas and vacuum flows may also be a patient safety issue. The variability is due to the lack of compliant source systems and engineering of the gas plumbing. Connecting anesthesia machines, through the use of both gas supply and vacuum fittings and adaptors that allow connection to a Category 3 system could potentially cause fluctuations in the fresh gas and vacuum flows to the machine. The change in vacuum flow could potentially cause increases in positive end expiratory pressure (PEEP) as vacuum levels decrease with concomitant use of the dental vacuum. Inappropriate fresh gas piping sizes could lead to inadequate flows, especially when using the oxygen flush valve. These technical issues rarely cross the mind of anesthesia professionals, as they are accustomed to appropriately designed systems in the hospital.

NFPA 2018 EDITION

The NFPA released the NFPA 99 Healthcare Facilities Code 2018 Edition in November of 2017. The NFPA worked with the American Dental Association and dental specialty groups to develop the latest edition. The lack of knowledge and adoption of code standards in dentistry was recognized by the NFPA. For example, The American Academy of Oral and Maxillofacial Surgeons (AAOMS) requires that all "AAOMS fellow/members must have their offices successfully evaluated and re-evaluated by their component society every five years or in accordance with the state law, provided that the state law does not exceed six years between evaluations and otherwise meets AAOMS office anesthesia guidelines."[4] However, AAOMS Parameters of Care[5] are silent on NFPA 99 adherence. Individual state dental board requirements are also highly variable and do not discuss NFPA 99 requirements. Therefore, NFPA 99 has explicitly included dental offices in Chapter 15 "Dental Gas and Vacuum Systems."[6] The NFPA decided to explicitly include dental facilities in their own chapter to address the issues discussed above. However, they did not "grandfather" in existing systems in dental offices. Instead, NFPA 15.1.5 states, "An existing system that is not in strict compliance with the requirements of this code shall be permitted to continue in use as long as the authority having jurisdiction has determined that such use does not constitute a distinct hazard to life."[7]

NFPA 99 AND ANESTHESIA IN DENTAL PRACTICES

New dental offices should be aware of these new standards. The major dental equipment suppliers often offer design services, but are not well versed in medical gas systems. Local building inspectors often do not inspect dental offices for compliance unless the office specifically states that they offer certain sedation and anesthesia services. Professional engineers may be needed to design the gas system and mechanical closet. The thorough testing of medical gas systems is imperative as it ensures proper functionality of gas manifolds, alarms, and automated switchover valves and ensures against system leaks and medical gas line crossovers. This testing ensures that the medical gas system is performing properly much like a biomedical technician certifies the working order of anesthesia machines. The redundancy of these systems allows for additional patient safety and verification. For example, the requirement[8] during general anesthesia for an in-line oxygen analyzer on anesthesia machines serves as a protection against delivery of a hypoxic gas mixture in the event of a gas line crossover. The American Dental Association's Guidelines for the Use of Sedation and General Anesthesia by Dentists also requires either an in-line oxygen analyzer or "a functioning device that prohibits the delivery of less than 30% oxygen."[9] Of course, these devices may only be relied upon with adequate verification of the medical gas system installation, which is required by NFPA 99.

CONCLUSION

Existing offices should understand the regulatory issues included in NFPA 99 and the relevant society guidelines when introducing new sedation and anesthesia services. An existing Category 3 medical gas system is not permissible when adding sedation and anesthesia services, just because the system is already present at the dental office. This also applies when independent anesthesia professionals are brought into the office to assist in treatment of patients. In addition, offices providing sedation and anesthesia without the proper independent third-party certification of their gas system, may, at the very least, be responsible for notifying the authority having jurisdiction of such. As one state-level AHJ and professional engineer stated, "This, however, does not relieve the building owners, contractors, architects, engineers, material suppliers, and anyone involved including the dental practitioners in the construction of the medical gas systems from complying to this code (personal communication)." The best practice is to ensure that an independent ASSE 6030 medical gas verifier has evaluated the medical gas system for any new installation or repair and whenever adding additional sedation or anesthesia services to any office or facility. Although not required by the NFPA, routine maintenance and certification of the gas system is also recommended, just as it is for anesthesia machines.

Dr. Wong is a dentist anesthesiologist in private practice at Coastal Pediatric Dental & Anesthesia in Norfolk, VA.

Gerhard Gschwandtner is a professional engineer, certified health care safety professional, and credentialed medical gas verifier at Comprehensive, Inc in Cary, NC.

Both authors have no disclosures relevant to the content of this article.

Special acknowledgment to Dr. Jan Ehrenwerth for serving as guest editor. Dr. Ehrenwerth presently serves on the APSF editorial board.

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8 Standards for basic anesthetic monitoring. American Society of Anesthesiologists Committee of Standards and Practice Parameters; 2015, p. 2.
9 Guidelines for the use of sedation and general anesthesia by dentists. Chicago, IL: American Dental Association; 2016; p. 10 & 13.

Dear SIRS:
SAFETY INFORMATION RESPONSE SYSTEM

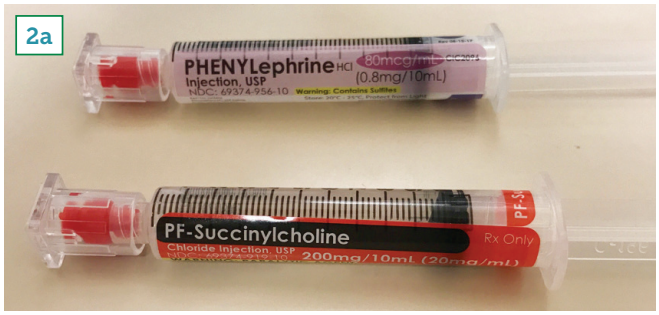
"No Read" Errors Related to Prefilled Syringes

Dear SIRS:

Prefilled syringes provide considerable benefit to anesthesia professionals including sterility, convenience, affordability, and perceived safety.[1] At our institution, we use syringes from multiple manufacturers and have realized several of the benefits above. Here, however, we report a pair of "no-read" medication administration errors related to prefilled syringes of phenylephrine and succinylcholine manufactured by Nephron Pharmaceuticals Corporation (Columbia, SC). The first event involved a patient accidentally receiving 40 mg of intravenous (IV) succinylcholine for hypotension during the process of moving to the operating room table. The patient suffered no apparent long-term consequences, but became apneic and was paralyzed without anesthesia. Following a department-wide Morbidity and Mortality conference shortly after this event, another patient was accidentally administered IV 480 mcg (6 ml) phenylephrine after induction of anesthesia instead of 120 mg (6 ml) succinylcholine. No-read errors are primarily the responsibility of the care provider team. However, we determined that the specific packaging of the syringes and the associated potentially dangerous visual similarity of the specific products may also contribute to the drug error (Figures 1a and 1b). The present syringes meet the ASTM standards, but the lack of circumferential red color around the succinylcholine syringe may lead to accidental administration of a paralytic.[2] To address this present issue, our pharmacy placed a paper label on the succinylcholine syringes. However, this negates the purpose of purchasing prefilled and pre-labeled syringes. In addition, it may create new threats of drug error and associated morbidity.

The authors partnered with the APSF and Nephron Pharmaceuticals, who efficiently acknowledged the problem and created new labels (see Figures 2a and 2b) that we believe will help prevent this pattern of drug administration errors. We appreciate the support and ethos that APSF provided to our concern and the responsiveness by Nephron Pharmaceuticals.

See "Dear SIRS," Next Page



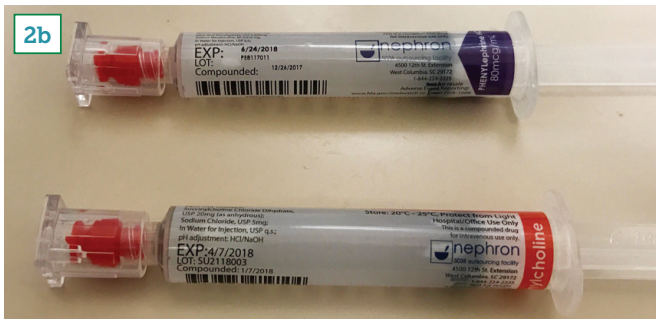


Figure 1a: Front, 1b: Reverse: original syringes of phenylephrine (top) and succinylcholine (bottom). Note lack of circumferential red coloration on succinylcholine, reducing visual discrimination of commonly used syringes.

Figure 2a: Front, 2b: Reverse: redesigned syringes with different barrel color and circumferential red band.

Dear SIRS refers to the **S**afety **I**nformation **R**esponse **S**ystem. The purpose of this column is to allow expeditious communication of technology-related safety concerns raised by our readers, with input and responses from manufacturers and industry representatives. Dr. Jeffrey Feldman, current chair of the Committee on Technology, is overseeing the column and coordinating the readers' inquiries and the responses from industry.

Dear SIRS SAFETY INFORMATION RESPONSE SYSTEM

Change in Prefilled Syringe Labels

From "Dear SIRS," Preceding Page

William R. Hand, MD, FASA
Vice-Chair of Academics
Department of Anesthesiology
University of South Carolina School of Medicine. Greenville, SC

Vito Cancellaro, MD
Chairman Department of Anesthesiology
Greenville Health System
Greenville, SC

Neither author has any relevant disclosures related to the content of this letter.

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Reply:

Nephron Pharmaceuticals is a firm with over 20 years of sterile pharmaceutical manufacturing experience. We appreciate the work of Dr. Hand, Dr. Cancellaro, and APSF Editor-in-Chief, Dr. Greenberg. Our syringe labels were enhanced using our in-house digital printing press, and quickly deployed to the entire US hospital market. As a market leader in prefilled syringes for anesthesia use in US hospitals, the Nephron CGMP quality team continuously monitors all aspects of product quality. We welcome input from the dedicated professionals working with APSF.

Sincerely,
Lou Kennedy
Chief Executive Officer
Nephron Pharmaceuticals Corporation

LETTER TO THE EDITOR:

In Response to "Carbon Dioxide Used as Insufflating Gas May Raise $ETCO_2$ During GI Endoscopy"

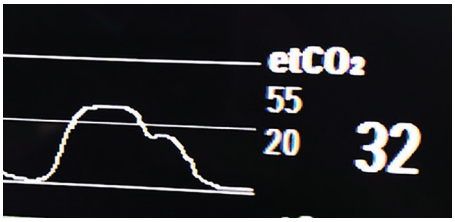
To the Editor:

We commend Dr. Berry for his insightful Letter to the Editor regarding carbon dioxide (CO_2) insufflation during GI endoscopy in the February 2018 A*PSF Newsletter.* GI endoscopists are moving from air to CO_2 as their choice of insufflating gas to facilitate endoscopy. Dr. Berry warns the readership of real consequences:

1) The possibility of elevated measured end-tidal CO_2 (sometimes >80 mmHg).
2) Significant absorption of CO_2 in tissue and the vascular system during long procedures, leading to a drop in the pH.

However, even a $PaCO_2$ of 130 to 160 mmHg (even up to 250 mmHg), in healthy volunteers, has been shown to be well tolerated.[1] In the case of gastrointestinal endoscopy, the clearance of insufflated CO_2 from the gut is much more rapid than it is for air. The American Society of Gastrointestinal Endoscopists (ASGE) has published a Technology Status Evaluation Report that discusses in depth the risks and benefits of CO_2 insufflation.[2] A robust bibliography is cited, and 36 randomized controlled trials (RCTs) are discussed that speak to the high safety profile for CO_2 insufflation.[2] Most of these excluded patients with pulmonary disease, yet three studies did compare CO_2 insufflation in healthy patients versus patients with subclinical pulmonary dysfunction or actual COPD. These studies showed no difference in the rate of CO_2 rise, peak CO_2, or SpO_2, but one showed a positive correlation for risk of CO_2 retention with increased procedure time. Dr. Berry is right to warn providers about the associated CO_2 elevations during longer endoscopy procedures. The study he mentions, Suzuki 2010 et al.,[3] involves a specialized, advanced endoscopy procedure (esophageal endoscopic submucosal resection), with a median duration of 122 minutes and a rise in median $PaCO_2$ value from a baseline of 28 mmHg to a peak $PaCO_2$ of 39 mmHg. Thankfully, most upper endoscopies are far shorter (somewhere around 4 to 9 minutes).[4,5] They can often be accomplished, as is largely the European experience, under minimal to moderate conscious sedation, or even under no sedation. Current evidence suggests that CO_2 insufflation is safe even in patients with COPD, but further RCTs would be helpful. Dr. Berry sagely advises caution and increased vigilance.

Respectfully yours,
Jeffrey D. White, MD
Associate Professor of Anesthesiology
Medical Director of Non-OR Anesthesia
Associate Medical Director of GI Endoscopy
Department of Anesthesiology
University of Florida College of Medicine



Joshua W. Sappenfield, MD
Assistant Professor of Anesthesiology
Director, Airway Management Rotation
Medical Director of the Preoperative Clinic
Chief of the Perioperative Medicine Division
Department of Anesthesiology
University of Florida College of Medicine

The authors have no disclosures as they pertain to this article.

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Companies support the APSF in many ways. Pharmaceutical, medical device, related organizations, and anesthesia practice management companies make it possible for the APSF to fulfill its mission to continually improve the safety of patients during anesthesia care by encouraging and conducting:

- safety research and education;
- patient safety programs and campaigns;
- national and international exchange of information and ideas.

With your generous contributions, the APSF can achieve its vision that no patient shall be harmed by anesthesia.

If your organization is interested in partnering with the APSF to support patient safety, contact the APSF office at moser@apsf.org or warner@apsf.org

PARTICIPATE IN THE 2018 APSF CORPORATE ADVISORY COUNCIL

The Anesthesia Patient Safety Foundation invites you to become a member of our 2018 Corporate Advisory Council (CAC). When your company becomes a member of the CAC, in addition to the benefits of membership, your company will also be recognized as a supporter of the mission of APSF. Some of the benefits of membership, depending on your level of support and participation, include

- Invitations to participate in the CAC meetings and conference calls, and to meet in person once a year to discuss topics pertinent to patient safety and industry
- Recognition in APSF communications, online and in print
- Invitation to APSF events and meetings with executive-level leadership
- Research and collaboration opportunities
- Networking opportunities allowing leaders from corporations and APSF to share ideas and information.

For specific information about the benefits of corporate membership, please contact Sara Moser at moser@apsf.org.

OPPORTUNITY TO SPONSOR APSF STOELTING CONSENSUS CONFERENCE

The Stoelting Conference, formerly known as the Consensus Conference, brings a defined group of approximately 125 leaders from perioperative professional organizations such as the American Society of Anesthesiologists (ASA), the American Association of Nurse Anesthetists (AANA), the Association of Operating Room Nurses (AORN), the American Society of PeriAnesthetic Nurses (ASPAN), and surgical societies together with representatives from anesthesia-related industries and colleagues from insurance, human factors, and legal fields. The recommendations from these conferences have led to significant practice changes resulting in improved patient safety. Examples include perioperative fire safety, vision loss, residual neuromuscular blockade, and operating room distractions. The 2018 Stoelting Consensus Conference is September 5–6, 2018, at the Royal Palms Resort in Phoenix, AZ and is entitled "Perioperative Medication Safety—Advancing Best Practices."

Maximum Number of Stoelting Conference Supporters: Four

For more information about the benefits of sponsoring the Stoelting Conference, please contact Sara Moser at **moser@apsf.org**.

SPONSORSHIP OF TRANSLATIONS OF THE *APSF NEWSLETTER*

One of APSF's key initiatives is to improve the international exchange of patient safety information and ideas. To accomplish this in 2018, we are working with our colleagues and industry partners to make perioperative patient safety information, guidelines, and recommendations easily obtainable worldwide. The seven translated languages will include Chinese, Spanish, Portuguese, French, Arabic, Russian, and Japanese. Data from the World Health Organization suggest that 95% of the world's anesthesia professionals will comprehend articles in English or in one of these languages.

For more information on sponsoring a newsletter translation, please contact Sara Moser at moser@apsf.org.


—A TRANSLATION FROM ENGLISH COMMISSIONED BY THE ANESTHESIA PATIENT SAFETY FOUNDATION—

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The Official Journal of the Anesthesia Patient Safety Foundation

SELECTED ARTICLES FROM THE APSF NEWSLETTER NOVEMBER 2017

Anesthesia Patient Safety Foundation（APSF）は、日本麻酔科学会（JSA）と連携し、日本語版APSFニュースレターを作成し、配布することにしました。JSAの安全委員会がこの企画を担当します。共通した目標は、周術期の患者の安全教育を改善することです。APSF Newsletterの読者は、127ヶ2千人以上おりますが、各国で25万人までの拡大を目指しています。今後は、さらにスペイン語、中国語、ポルトガル語、アラビア語、ロシア語の5か国語で発行する計画があります。このプロジェクトの日本における第1版をこの方法で出版できる運びとなりました。今後も、充実した内容になるように努めてまいりたいと思います。

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Department of Anesthesiology and Intensive Care Medicine
Nagoya City University Graduate School of Medicine

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Steven Greenberg, MD, FCCP, FCCM
Editor-in-chief of the APSF Newsletter
Clinical Associate Professor in the Department of Anesthesiology, Critical Care at the University of Chicago, Chicago, IL.
Vice Chairperson, Education in the Department of Anesthesiology at NorthShore University HealthSystem, Evanston, IL.

Edward Bittner, MD, PhD, MSEd
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Associate Professor, Anaesthesia, Harvard Medical School
Department of Anesthesiology, Critical Care and Pain Medicine
Massachusetts General Hospital, Boston, MA.

Jennifer Banayan, MD
Assistant Editor, APSF Newsletter
Assistant Professor,
Department of Anesthesia and Critical Care
University of Chicago, Chicago, IL.

First Japanese edition of selected articles was published in November 2017.

Opportunity to Partner with APSF on Patient Safety Research Grants

The APSF has distributed $12 million in funding for anesthesia patient safety research projects over its 30-year history, leading to important discoveries that have changed clinical practices, improved patient outcomes, and supported the career development of anesthesia patient safety scientists. The results of these research grants have made significant contributions to the specialty.

For more information on sponsoring a research grant, please contact Sara Moser at moser@apsf.org.

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Special recognition and thanks to Medtronic for their support and funding of the APSF/Medtronic Patient Safety Research Grant ($150,000).

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Dear SIRS:
SAFETY INFORMATION RESPONSE SYSTEM

Not All Manifolds are the Same: Lessons in Intravenous Drug Administration

Dear SIRS:

I am writing to describe an incident we experienced at The University of Texas MD Anderson Cancer Center that has implications for providers administering intravenous medications, particularly in the operating room. In order to add port sites to a blood set, a Quest Medical six channel manifold was placed in line and a stopcock was placed in the tubing between the patient and the manifold (Figure 1). Later in the case, blood was administered during an episode of hypotension and a 20ml syringe was connected to this stopcock to act as a pump, allowing the periodic aspiration and injection of blood. A sudden increase in blood pressure was seen and it was noted that a syringe of phenylephrine that had been left on the manifold was now empty. It was determined that 2ml of phenylephrine (100mcg/mL) had inadvertently been administered to the patient. The blood pressure response was temporary, within 20% of the patient's baseline blood pressure, and started to fade within minutes.

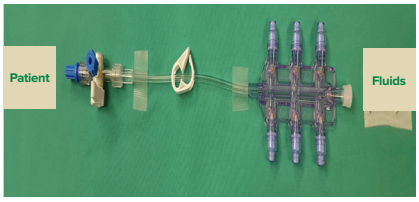


Figure 1: Set up of iv tubing, manifold, and downstream stopcock that could potentially allow for inadvertent aspiration if performed at the level of the stopcock and syringes are freely connected to the manifold.

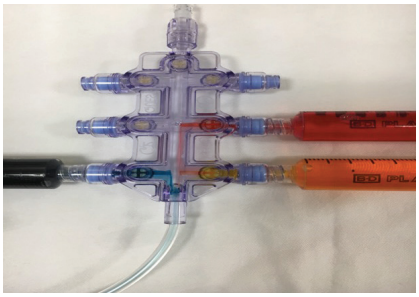


Figure 2: Aspiration downstream allowing the contents of multiple syringes connected to an in-line manifold to be drawn inside the iv tubing.

Providers should be aware that the possibility of downstream aspiration of medications is possible when syringes are left connected to certain types of manifolds, especially those without built in stopcocks. Figure 2 shows various colored dyes being pulled into a manifold when aspiration is performed downstream. Figure 3 demonstrates how contents from syringes left on manifolds with stopcocks (orange/red dyes) do not allow for downstream aspiration, while aspiration is possible with manifolds without stopcocks that have syringes freely connected to them (blue dye). This could lead to clinically important consequences, such as unintended medication administration. Providers should practice vigilance and disconnect any syringes from manifolds/port sites that are not actively being used to administer medications.

Ravish Kapoor MD
Assistant Professor
Department of Anesthesiology
& Perioperative Medicine
The University of Texas MD Anderson Cancer Center

Reply:

A unique method for actively pumping blood in an IV line has been demonstrated, which contained our MultiPort® manifold. A syringe containing phenylephrine drug was attached to the manifold. A second syringe was attached to the IV line downstream from the manifold and used as a "pump" to create negative pressure, which resulted in the liquid from the phenylephrine syringe being introduced into the IV line. The check valves incorporated into the MultiPort device are passive, or a "floating disc" design, which simply open or close based on a pressure differential. The purpose of a passive check valve is to prevent drugs/fluids injected from one port from entering another port on the manifold. A passive check valve will not prevent positive flow if a vacuum condition is created downstream from the manifold. Quest Medical concludes that the device performed as intended. Quest Medical does offer alternative manifolds that incorporate the use of positive pressure valves, which may be more suitable for your unique method of use. Thank you for providing feedback on the use and performance of our products. Our objective is to provide high quality medical devices. Your input is valuable in support of Quest Medical's goal of continuous improvement.

Jan Hodges
Director, Quality Assurance & Regulatory Affairs
Quest Medical, Inc.

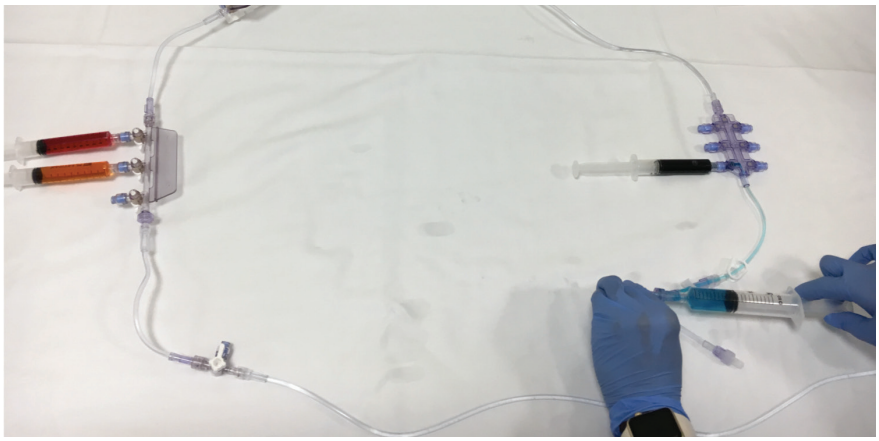


Figure 3: Notice how contents of syringes connected to manifold with stopcocks are not aspirated downstream (orange/red dyes), but aspiration of contents from syringe attached to manifold without stopcocks is possible (blue colored dye).

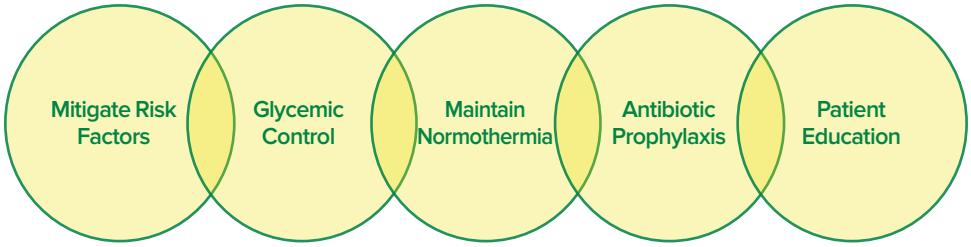
Preventing Surgical Site Infection After Cesarean Delivery—The Anesthesia Professional's Role

by: Katherine M Seligman, MD; Daniel Katz, MD; Michaela K Farber, MD

I. BURDEN OF SURGICAL SITE INFECTIONS

Surgical site infections (SSIs) represent a significant portion of health care morbidity and expense in the United States (US). While SSIs complicate 1.9% of all surgeries performed, the incidence of SSI after cesarean delivery (CD) is substantially higher, 7-10%.[1-3] As CDs are the most common surgery performed in the US (>1.2 million performed per year), post-CD SSI is a significant cause of increased morbidity, mortality, readmission, and prolonged hospitalization.[4] The estimated cost burden for SSI after cesarean delivery is $2852–$3842 per case in the US.[5] Recognition and implementation of evidence-based initiatives with a bundle approach to prevent and reduce SSI after CD may aid in optimizing maternal safety, while reducing cost.

Figure 1: Bundle components can work synergistically to decrease rates of surgical site infections and improve patient outcomes.



II. CLASSIFICATION AND RISK FACTORS OF SSI

Surgical site infections include superficial and deep incisional infections as well as organ space infections.[1] Incisional infection after CD occurs in 2-7% of cases; necrotizing fasciitis in 0.18%; and endometritis in 2-16%.[6] The CDC has released guidelines for the classification and surveillance of SSIs diagnosed within 30 days of surgery.[1,7,8]

Identification of risk factors for the development of SSIs after CD may help define modifiable points in obstetric care and lower the incidence of SSIs.[7] Patient-related risk factors include elevated BMI, diabetes, asthma, smoking, recurrent pregnancy loss, and ASA classification >3.[9-11] There is myriad evidence in the general surgical literature that glucose control and smoking cessation decrease rates of surgical site infection.[12,13] To our knowledge, impact of these interventions in the pregnant population has not been reported. Pregnancy-specific risk factors include hypertensive disorders, gestational diabetes mellitus, prolonged rupture of membranes, prolonged labor, sexually transmitted infections in pregnancy, chorioamnionitis, and multiple gestations.[9-11] Procedure-related risk factors include increased operative time (> 38 min), bowel injury, use of staples, non-closure of subcutaneous tissue if greater than 2 cm, and the inappropriate use of perioperative antibiotics.[9-11,14] Emergent CD has been implicated, but has not been directly correlated with increased risk for SSI.

Table 1: Sample SSI Bundle and Phase of Care

Intervention	Phase of Care
4% Chlorhexidine Gluconate shower x 2[33] night before & morning of surgery	Pre-Op
Hair removal with clippers[34] immediately before entering OR	Pre-Op
Glycemic control Blood glucose < 126 mg/dl* (Pre-op, Intra-op)[17] Blood glucose < 200 mg/dl (Post-Op)[8,18]	Pre-Op, Intra-Op, Post-Op
Appropriate antibiotic administration within 1 hour of skin incision*[21,22] < 120 kg – 2 g Cefazolin ≥ 120 kg – 3 g Cefazolin + 500 mg Azithromycin if ruptured membranes	Pre-Op
Maintain normothermia, maternal temp. > 36°C*[26]	Pre-Op, Intra-Op, Post-Op
Chlorhexidine with alcohol skin prep[35]	Pre-Op
Providone Iodine vaginal prep[36]	Pre-Op
Umbilical cord traction for placental delivery[37]	Intra-Op
Antibiotic re-dosing if EBL > 1500 mL or time > 4 hrs[23]	Intra-Op
Glove change prior to fascia closure[38]	Intra-Op
Subcutaneous tissue closure with suture for depth > 2 cm[39]	Intra-Op
Skin closure with suture[35]	Intra-Op
Dressing removal between 24–48 hrs[8]	Post-Op
Patient education on wound care & signs of SSI*[32]	Post-Op

* Indicates where anesthesia professional may have a collaborative role in the interventions.

III. DEVELOPING A SSI BUNDLE

The Institute for Healthcare Improvement introduced the concept of "bundles" as a way to adopt evidence-based guidelines into practice to improve patient outcomes and care (Figure 1).[15] Institutions that have implemented SSI bundles to decrease rates of infection following CD have seen statistically significant decreases in postoperative complications.[5,16] Although surgeons dictate most of the interventions to decrease SSI, there are a few important circumstances where the anesthesia professional may intervene. The following section will outline evidence-based bundle components that an anesthesia professional may implement to decrease SSIs. An example bundle containing nursing, surgical, and anesthesia components is shown in Table 1.

See "SSI," Next Page

Proposed Cesarean Section SSI Prevention Bundle Elements

From "SSI," Preceding Page

GLYCEMIC CONTROL

Peripartum normoglycemia for women with diabetes is associated with improved fetal and maternal outcomes. Conversely, perioperative hyperglycemia is a noted risk factor for post CD SSI.[5,9] Further benefits to maintaining a normal range of maternal glucose (70–126 mg/dL) include lowering the risks of neonatal hypoglycemia and maternal ketoacidosis.[17] Women with a diagnosis of diabetes should have a blood sugar evaluated preoperatively. Elevated blood glucose should be treated with insulin. If a patient receives insulin, blood glucose should be re-evaluated within 30–60 minutes of administration.[18] If the surgical procedure is >1 hour in duration, a bedside glucose level can be obtained intraoperatively to guide treatment. A blood glucose level should also be obtained in the PACU.[19] According to the CDC guidelines, a more liberal yet controlled postoperative glucose target of < 200 mg/dl may decrease morbidity associated with hypoglycemic events and strict glycemic control, while still potentially reducing rates of SSI. However, these data originated from the non-obstetric surgical population, and further studies for post-cesarean delivery patients are warranted.[8,18,20]

PREOPERATIVE ANTIBIOTICS

The American College of Obstetricians and Gynecologists (ACOG) guidelines recommend the administration of a first generation cephalosporin within 1 hour prior to incision, dosed according to maternal body weight (cefazolin 2 g IV if <120 kg; cefazolin 3 g IV if ≥120 kg). The previous practice of dosing antibiotics after cord clamping has been shown to increase rates of infection and should be abandoned.[21] A recent study suggests that azithromycin 500 mg IV administered prior to incision in non-elective CD, in addition to a cephalosporin, decreased the rate of SSI by half.[22] However, further validation with assurance of primary cephalosporin coverage will be important to refine the target population who will most benefit from this adjunct. Patients with anaphylaxis to penicillin can receive clindamycin 900 mg IV and gentamycin 5 mg/kg IV (dosing weight) prior to incision, although local antibiotic resistance patterns may dictate the use of vancomycin or other antibiotics depending on these patterns.[21] The re-dosing of prophylactic antibiotics in the setting of postpartum hemorrhage defined as >1500 mL estimated blood loss, and also after two half-lives of the medication have passed, are additional strategies that may reduce post-CD SSIs.[23] Further studies are required in the parturient population to definitively validate these redosing recommendations.

NORMOTHERMIA

Perioperative hypothermia is associated with increased wound infection, length of hospital stay, and increased morbidity and mortality for premature infants.[24,25] Maternal temperature should be monitored intraoperatively and postoperatively with a goal perioperative maternal temperature of >36.0 °C per WHO guidelines.[26] The anesthesia professional may consider a temporal thermometer or foley temperature probe as the patient is awake. Skin temperature probes can vary from core temperature by 0.5-2 °C and may be used taking this into account.[27] The use of forced air warmers and increasing operating room temperature have been shown to decrease rates of perioperative hypothermia in parturients and neonates.[28,29] The anesthesia professional may consider setting the OR temperature to 22.5 °C (72 °F) and placing an upper and/or lower body forced air warmer to ensure normothermia is maintained.[8] Intraoperative temperature may also be obtained every 15–30 minutes and documented.[30]

PATIENT EDUCATION

SSI prevention requires adherence to guidelines by surgeons, nurses, and anesthesia professionals as well as participation by patients and their families.[31] Patient education surrounding postoperative wound care, appropriate hand hygiene for patient/staff/family, and signs of infection should be delivered preoperatively as well as postoperatively.[32] The anesthesia professional may emphasize strict adherence to hand washing and be vigilant about detecting early signs of infection that may occur at any point of their patient interaction, such as fever, tachycardia, vasopressor requirement, or leukocytosis.

IV. CONCLUSION

Evidence-based interventions that demand a multidisciplinary team approach have proven effective for decreasing the incidence of post-CD SSIs.[31] Integrating change in a hospital system, from identifying evidence-based measures that reduce post-CD wound infections to the final step of applying and tracking such measures, works best if a team approach is used integrating obstetrics, anesthesia, nursing, and quality. The ultimate goal of a SSI bundle is to eliminate deviations from standard of care and decrease maternal morbidity and mortality. Further research is required to determine which set of interventions optimize improvement in patient outcomes.

Dr. Seligman is an Assistant Professor and Division Chief of Obstetric Anesthesia in the Department of Anesthesiology and Critical Care Medicine at the University of New Mexico.

Dr. Katz is an Assistant Professor in the Department of Anesthesiology, Perioperative & Pain Medicine at Icahn School of Medicine at Mount Sinai in New York.

Dr. Farber is an Assistant Professor, Obstetric Anesthesia Fellowship Director, and Associate Division Chief of Obstetric Anesthesia in the Department of Anesthesiology, Perioperative & Pain Medicine at Brigham and Women's Hospital in Massachusetts.

None of the authors have any disclosures.

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Cesarean Delivery SSI Prevention Bundle

From "SSI," From Preceding Page

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ANNOUNCEMENT

APSF Safety Recognition Award

Best Practices for Safe Medication Administration during Anesthesia Care

Deadline for Submission: June 15, 2018

The Anesthesia Patient Safety Foundation seeks to recognize organizations that have made significant advances in safe medication administration during anesthesia care. Best practices of safe medication administration covered by the STPC paradigm*—Standardization, Technology, Pharmacy, Culture—will be considered. Special consideration will be given to practices with processes that complement patient care workflow and integrate documentation with the EHR. Evidence indicating improved medication safety is most desirable, but it is recognized that qualitative evidence of process improvement (e.g., surveys of user acceptance) may be the best available evidence. Actual implementation experience in patient care is also required rather than ideas that have yet to be implemented.

Submissions should be limited to 1500 words and include the following:

- A description of the objective(s) of the practice including the aspect(s) of the STPC approach that are incorporated
- A description of the clinical workflow designed to support the practice
- Integration with the electronic health record
- The duration of time the practice has been in use
- The approximate number of patients impacted since implementation
- Methods used to evaluate effectiveness

Awardees will be invited to the upcoming Stoelting Conference on Medication Safety in Anesthesia to be held September 5, 2018, in Phoenix, AZ, to receive the award and present their work. They will also be recognized with a certificate from the APSF and publication of their work in the *APSF Newsletter*, website, and social media feeds. Submissions will be reviewed by members of the APSF Committee on Technology. The award will be approved by the APSF Board of Directors and announced by August 1, 2018.

Award Applications should be submitted to Yulonda Motley, Assistant to Jeffrey M. Feldman, MD, Chair, APSF Committee on Technology at motleyy@email.chop.edu.

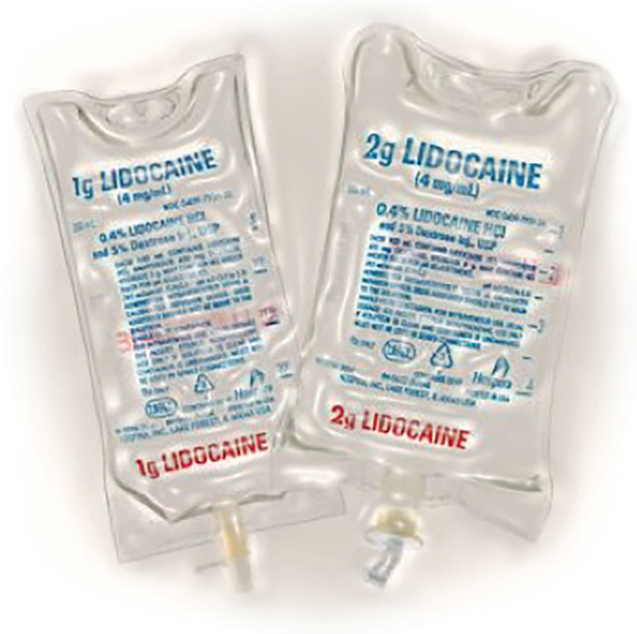
*STPC Paradigm: https://www.apsf.org/resources/med-safety/

Systemic Lidocaine: An Effective and Safe Modality for Postoperative Pain Management and Early Recovery

by Brent Earls, MD, and Lisa Bellil, MD

Since its development in 1943, lidocaine has been a versatile medication in the armament of the anesthesia professional. Originally used as an anti-arrhythmic drug, it wasn't long before its impact on pain was discovered.[1] The earliest articles published showing pain reduction came out in the 1960s. Possibly due to the current opioid epidemic or perhaps because of the adoption of early recovery protocols and the concept of multimodal surgical care, lidocaine for analgesia has seen a re-emergence. From use in chronic pain syndromes to open abdominal surgery, lidocaine infusions have been incorporated and found to have positive results with a well-tolerated side effect profile. The antinociceptive properties of systemically administered lidocaine have repeatedly been shown in various experimental and clinical pain conditions.[2-5] Some literature suggests that systemic administration of lidocaine may confer anti-metastatic benefits in some cancer patients.[6] Studies have shown lidocaine to have a glycine-like action in the central nervous system at plasma levels far below what is required to prevent nerve impulse generation. The role of lidocaine in chronic inflammatory conditions is a much more recent area of research. Changes in expression of sodium-channel isoforms are involved, and lidocaine is believed to have its effect at these sites in the dorsal root ganglion.[7] Additionally, lidocaine has been shown to modulate N-methyl-D-aspartate (NMDA) receptors, which could contribute to the prevention of chronic pain states.[8,9] The therapeutic index of lidocaine has been investigated by several researchers and found to have optimum effects at 2–10 µg/mL[2] and a total duration of 24–48 hours from the start of the infusion. Achieving and maintaining this level can be dependent on patient co-morbidities, age, and other factors that should be considered on a patient-by-patient basis.[10]

Lidocaine infusions have influenced numerous clinical outcomes investigated by researchers. Terkawi et al. conducted a trial including 216 patients and found lidocaine infusion to be equal with respect to pain scores to epidural analgesia in adults undergoing abdominal or pelvic surgery. They also found lower incidence of postoperative nausea and vomiting, pruritus, and urinary retention. However, the intravenous lidocaine group, receiving 1 mg/kg per hour for up to 96 hours postoperatively did have higher systemic opioid consumption when compared to the epidural analgesia group, who received a combination of 0.125% bupivicaine and



10 micrograms per milliliter of hydromorphone through the epidural.[11] It comes as no surprise that thoracic and lumbar epidural analgesia does provide better pain relief at late time points, although studies are showing intravenous (IV) lidocaine to be a great alternative in patients who refuse neuraxial methods or have contraindications and can provide great analgesia up to two days after surgery.[11-13]

When administering a lidocaine infusion, it is important to discuss this plan with the surgical team prior to administering the infusion as well as to check for any contraindications in each patient (Table 1). Fortunately, lidocaine has a long-proven track record for safety as an IV medication and has been very well tolerated in the trials investigating the efficacy of this method.[12,14,15]

In 2015, a Cochrane review, which included 45 trials, was published comparing the effect of continuous perioperative lidocaine infusion either with placebo, or no treatment, or with epidural analgesia in adults under general anesthesia. The epidurals contained various solutions of dilute local anesthetics with or without low-dose opioids. The results suggested that the lidocaine infusion group had a reduction in postoperative pain at early and intermediate time points, expedited gastrointestinal recovery time, reduced postoperative nausea/vomiting and opioid usage as well as a reduction in hospital length of stay.[16] There was limited data on adverse effects in the studies with the lidocaine intervention. However, most reported events were limited to light-headedness, tinnitus, or headache. There were no serious adverse events reported from these trials or poor surgical outcomes related to the lidocaine infusion reported in the treatment arm of the trials reviewed. Despite the more than 40 trials included in the review, more high-quality evidence is needed to delineate the clinical effect that can be expected with this modality. The Cochrane review concluded that there was low to moderate evidence. The authors also noted a scarcity of studies evaluating optimal dose, adverse effects, and timing, and further research is likely to have an important impact on the confidence in the estimate of effect.[16]

Rimback et al. compared systemic lidocaine (3 mg/min) versus normal saline placebo in 30 patients undergoing elective cholecystectomy in the early 1990s. They found reduced need for opioids, earlier return of bowel function, and shorter hospital stays. This group proposed a mechanism of less peritoneal irritation thus reducing inhibitory gastrointestinal reflexes.[14] Several randomized, placebo-controlled clinical trials have demonstrated that IV lidocaine administration similarly reduces the duration of postoperative ileus and need for narcotic pain control, thus accelerating hospital discharge.[12,14,15,17] In this early study, Rimbäck et al. implied that lidocaine infusions might reduce inflammation by blunting the sympathetic response and the associated inflammatory cascade.

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Pain Programs May Manage Lidocaine Infusions Safely With Appropriate Monitoring

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Herroeder et al. performed a double-blind, randomized, controlled study in 60 patients undergoing colorectal surgery. Their results suggested that with systemic lidocaine (1.5 mg/kg bolus followed by a 2 mg/min infusion), patients were afforded shorter hospital stays and earlier return of bowel function. They were also able to show a measured reduction of a variety of inflammatory cytokines in the systemic lidocaine group.[15] This study was able to showcase not only the central analgesic properties of local anesthetics but also the anti-inflammatory properties. This significant reduction in inflammatory mediators has implications in not only return of bowel function and postoperative ileus but also thrombosis, postoperative myocardial infarction, and sepsis.[18]

At Medstar Georgetown University Hospital, we have eagerly adopted IV lidocaine infusions as part of a balanced anesthetic plan. Several surgeons regularly incorporate IV lidocaine infusions into their perioperative treatment protocols. It is used as a fundamental component of our early recovery protocol in combination with acetaminophen, gabapentin, and celecoxib. This protocol is incorporated into most patients' care undergoing colorectal surgery[19] or, cholecystectomy; however, it has been used successfully in select patients not undergoing abdominal surgery. Patients are evaluated on an individual basis for candidacy of each medication. A thorough history and physical exam are performed to rule out contraindications to lidocaine (Table 1).

During induction, the systemic administration is started with a one-time bolus of 1–1.5 milligrams per kilogram ideal body weight (IBW) after which time an infusion is initiated at 2 milligrams per kilogram per hour (IBW). This rate is continued for the first four hours and then reduced to 1 milligram per kilogram per hour for the remainder of the infusion period. Reducing the infusion rate after the first four hours is an effective and simple method to avoid toxic levels of lidocaine, but maintain a therapeutic concentration for pain control.[20] Biotransformation of lidocaine yields metabolites monoethylglycinexlidide (MEGX) and glycine xylidide (GX). The systemic actions of these metabolites are similar to, but less potent than, lidocaine itself and are most pronounced when combined with concomitant administration with lidocaine. Pharmacokinetics of these metabolites can be diminished in individuals with liver cirrhosis[21] and has even been developed as a more sensitive index than the Pugh score for liver dysfunction.[22]

Table 1: Contraindications for Lidocaine Infusion[26]

Sensitivity or allergy to lidocaine
Significant heart disease (i.e., 2nd or 3rd degree heart block, Exception: Patients with a pacemaker)
Severe cardiac failure (Ejection fraction < 20%)
History of Adams-Stokes, Wolff-Parkinson-White Syndrome or active dysrhythmia
Concurrent treatment with Class I antiarrhythmics or amiodarone use < 3 months
Severe hepatic impairment (bilirubin > 1.46 mg/dl)
Severe renal impairment (<30mL/min/1.73 m^2 or ESRD)
History of uncontrolled seizure
Acute porphyria

After the patients are brought to the recovery room, our acute pain service takes over the management of the lidocaine infusion. This is an important step in maintaining safety during the infusion period to have early recognition of local anesthetic toxicity. Our staff will monitor patients at least every four hours for lightheadedness or dizziness, visual and auditory disturbances, or metallic taste and are available at all times for any concerns. Unfortunately, our clinical laboratory processes serum lidocaine as a send-out laboratory value, and, therefore, it can take up to three days to obtain a result, which limits its use in clinical practice. Therefore, if our staff recognizes or has suspicion of early signs of toxicity, the infusion is discontinued and the patient is moved to an intermediate care unit for continuous telemetry. Our protocol utilizes the Checklist for Local Anesthetic Systemic Toxicity (LAST) published by the American Society of Regional Anesthesia and Pain Medicine.[23] As an additional precaution, the pharmacy will stock 20% IV fat emulsion in the automated medication dispensing system of floors where patients are receiving the infusion for quick access in case of emergency. Because lidocaine levels would not be processed in a clinically useful timeframe, it is important for us to recognize dangerous clinical signs and initiate treatment early. These signs include hypotension, seizure, loss of consciousness, and very late signs can include respiratory arrest and cardiac arrhythmia or arrest.[24] If these signs are witnessed or suspected, the acute pain service attending physician is immediately notified and will determine the need for lipid emulsion. To date, we have not had any severe complications using our lidocaine infusion protocol since its implementation in the fall of 2017. Trials published using infusion rates for pain control document very few minor symptoms, which are self-limiting. Patients have noted symptoms including light-headedness, dizziness, tinnitus, or metallic taste in their mouth that resolve soon after discontinuation of the infusion. At this time, we recommend patients be monitored on the floor with continuous pulse oximetry without the need for routine telemetry. The lidocaine infusion is continued for 24 to 48 hours from initiation, as this is in line with the optimal clinical effect reported in most published trials we have investigated.[11-15,17,18,25] Our acute pain service will continue to follow up for an additional day to provide an extra layer of patient safety and continue to assist with pain management as needed.

Dr. Earls is an R2 (PGY-2) anesthesiology resident at Medstar Georgetown University Hospital.

Dr. Bellil is Director of Obstetric Anesthesia, former Director of Acute Pain Service and Assistant Professor in the Department of Anesthesiology at Medstar Georgetown University Hospital.

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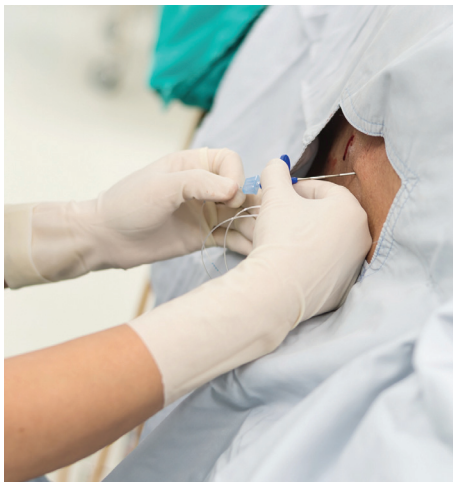
LETTER TO THE EDITOR:

A Bad System Will Beat A Good Person Every Time

To the Editor:

I read with interest the recent letter "**Flip-Flops** and Spinal Catheters" published in the February 2018 *APSF Newsletter*. In it, Dr. Schloemerkemper presents some practical system issues related to a resident placing a spinal catheter after an accidental dural puncture during placement of a labor epidural at her institution. Dr. Schloemerkemper focused on the resident's choice of an accepted, but unfamiliar technique. From a human factors engineering perspective, her solution: expect the resident to use better judgement in the future, should be reconsidered.[1] In fact, a closer look might reveal a system error being lack of supervision. I wonder, should we as anesthesia professionals treat the induction of labor epidural analgesia like we treat the induction of every other anesthetic and require an attending anesthesiologist to be in the room? I believe our job is to teach residents how to navigate unfamiliar situations, and laboring parturients deserve the same level of care as surgical patients.



Mark C. Norris, MD
Chief of Obstetric Anesthesia
Clinical Professor of Anesthesiology
Boston Medical Center
Boston, MA

Dr. Norris has no disclosures to report.

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In Response:

I thank the editors for allowing me to reply to Dr. Norris's comments. I agree with the quote indicating that a good person can be beaten by a bad system. Supervision can help defeat the odds and prevent a negative outcome. Nevertheless, the scenario I described highlights an issue that is independent of training experience or supervision. If we want to improve a "bad system," we have to identify it first. We also need to recognize that our work environment might differ from what we have read in the literature. Critically reflecting on the circumstances is something that needs to be encouraged, not just during residency but beyond. We have used the described scenario as a catalyst to create local guidelines regarding intrathecal catheter use.

Nina Schloemerkemper, MD, FRCA
Assistant Clinical Professor
Director of Neuroanesthesia Rotation
Department of Anesthesiology and Pain Medicine
UCDavis Medical Center, Sacramento, CA.

Disclosures: Dr. Schloemerkemper served as a consultant for Covidien and Mizuho OSI.

Dear SIRS:
SAFETY INFORMATION RESPONSE SYSTEM

Defective Pediatric Endotracheal Tubes (ETTs)

Dear SIRS:

I am writing to report a case of a defective pediatric endotracheal tube (ETT) that has implications for patient safety. A 14-day-old infant was induced intravenously for a sternal wound irrigation and closure and a 3.5 cuffed endotracheal tube was placed. A circuit leak resulted in inadequate ventilation, but despite checking all circuit connections from the machine to the endotracheal tube it could not be readily identified. Adding additional air to the endotracheal tube cuff did not perceptibly decrease the leak. Humidifiers tend to be a frequent source of circuit leaks, but all connections were intact in this case. An audible air leak sound was detected when listening closely to the patient's airway. Therefore, we removed the endotracheal tube from the airway and replaced it. Inspection of the tube showed a 3 mm diameter hole in the wall of the tube just proximal to the insertion of the pilot balloon (Figure 1).

We notified the anesthesia technicians who examined our stock of twelve more tubes with the same lot number. Close examination revealed that the "defect" proximal to the insertion of the pilot balloon was variable in size and depth in these tubes (Figure 2).

At least one of thirty-eight pediatric anesthesiologists in our group recalled a similar incident of difficult-to-isolate circuit leak, and it is possible that a similar ETT tube defect was missed.

An additional tube was found to have the same defect, approximately one and a half months after the initial defective ETT was found. A different lot number from the same manufacturer was noted on the packaging. This has led to a complete removal of 3.5 cuffed endotracheal tubes produced by this manufacturer and replacement with another product. The endotracheal tube defect specific to the manufacturer was submitted to the FDA and the manufacturer. We hope that this information is helpful to anesthesia professionals in a similar scenario.

Dr. Lindsey Loveland Baptist is Assistant Professor in the Department of Anesthesiology at the Medical College of Wisconsin and Associate Pediatric Anesthesiology Fellowship Director at Children's Hospital of Wisconsin, Milwaukee, WI.

Dr. Loveland Baptist reports no conflicts of interest.

Reply:

Upon receipt, Teleflex visually examined the endotracheal tube (ETT) and confirmed a hole in the tube, as originally reported. Teleflex was able to reproduce holes in other ETTs by excessively pressing the tube against the notch block during the manufacturing process.

Based on these findings, Teleflex has retrained all operators, implemented tightened sampling for the in-process inspections, inspected product in inventory (which found no nonconforming devices), and conducted a risk evaluation as per our internal procedures. Furthermore, Teleflex has opened a Corrective and Preventive Action (CAPA) Project to establish long-term corrective actions and prevent the recurrence of this failure by reducing variability in our manufacturing process.

Teleflex endeavors to manufacture its medical devices to the highest possible standards and has comprehensive, active quality systems in place to assure these standards. We are indebted to you for highlighting this issue with one of our devices. This report has enabled us to identify an area for improvement in our manufacturing process. We regret the occurrence of this incident and ask that anyone who experiences such an incident to please report it to us so that we can continuously assess our quality system performance and any needs for further investigation. Patient safety remains the focus of all that we do.

Lucas B. Elliott
Quality Assurance Lead
Customer Advocate Department
Teleflex Inc.

Figure 1: This figure depicts the defect hole in the pediatric endotracheal tube near the pilot balloon entrance point.

Figure 2: This figure depicts defect holes within multiple pediatric endotracheal tubes near the entrance point of the pilot balloon. The holes are of varying diameter.

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