PREVENTION: REVIEW ARTICLE

Pediatric sedation – evolution and revolution
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Introduction
Any review of the current state of pediatric sedation should recognize that we are in the midst of a dynamic time for this area of medicine. Sedation for children is provided by a wide range of specialists around the world. The variety of backgrounds and practice settings that researchers and thought leaders bring to this practice makes for a melting pot for ideas and methodologies. The changes that are currently occurring represent the end result of both a long period of thoughtful application and moderation (evolution) as well as some rapid changes that challenge our ability to acclimate in a timely manner (revolution). This paper will consider both of these categories of changes and review some important developments that fall into each.

Evolution
Pediatric sedation literature and the evolving role of the anesthesiologist
A discussion of the changes in pediatric sedation must include the recognition that this field is now a multispecialty practice in which anesthesiologists play a key, albeit not exclusive, role. Anesthesiologists have helped to improve the safety of pediatric sedation through the thoughtful application of the same concepts that improved safety in the operating room. The adoption of a systems approach to monitoring, recovery, and rescue has clearly improved care for children during sedation (1–3). In the United States, the Joint Commission recognizes the role of anesthesiologists in their handbook and website (http://www.thejointcommission.com). It has revised its assessment of the role of anesthesiologists only slightly over the last 15 years. During the 1990s, language in the Joint Commission standards clearly placed responsibility for all sedation in a given institution under the Department Chair of Anesthesiology. The current version of these standards (published in 2008) states that the Anesthesiology Department should play a key advisory role in sedation privileging and quality improvement, but stops short of charging the Chair with complete oversight responsibility.

In 2011, the Center for Medicaid and Medicare Services (CMS) in the United States weighed in on sedation practice and oversight (4). Their detailed advisory contains specific recommendations on qualifications for providers who deliver deep sedation and anesthesia. This document does not restrict deep sedation to anesthesiologists, but it does compel hospitals and...
medical centers to place all deep sedation and anesthesia under the direction of one physician. At most institutions, this is logically the responsibility of the Chair of Anesthesiology. To meet these CMS directives, the role of the Chair of Anesthesiology will need to evolve to accommodate the need to manage diverse resources that are multidepartmental.

The evolution of sedation as a multispecialty practice is typified by the output of academic papers involving pediatric sedation over the last ten years. A review of the literature reveals a change in the publication of peer-reviewed research papers and non-peer-reviewed articles on pediatric sedation. A survey of the articles published in the year 2000 and 2009 relating to pediatric sedation is presented in Table 1. While this compendium is not comprehensive and includes papers with a range of rigor and quality, it is representative of the distribution of published articles on pediatric sedation. Examination of these lists confirms that pediatric sedation remains a popular topic for investigators in a variety of specialties. The total number of studies published continues to grow rapidly; however, the distribution has subtly changed. While two of the top ten journals publishing pediatric sedation studies or articles were anesthesia related in 2000, none of the top ten are North American anesthesia journals in 2009 (only anesthesia-based journal is Annales Francaises d’Anesthesia et de Reanimation). There is no doubt that anesthesiologists continue to serve a critical role in providing sedation of children for tests and procedures outside the operating room, but the academic activity produced around this work has not kept pace with other specialties.

There are several possible explanations for this evolution. First, this may be because of the fact that anesthesiologists simply do not find it compelling to report on a series of pediatric sedation cases. Furthermore, many anesthesia-focused journals would not find a report on a series of propofol sedations during MRI scans original enough to publish. On the other hand, the same study submitted by other specialists to a journal outside of anesthesiology might be considered interesting and original work because propofol sedation is relatively new to their field and there is much less experience with its use in that specialty. Just as likely is the possibility that anesthesiologists do not see this field particularly ‘challenging’ or ‘interesting’ and many choose not to spend valuable academic energy in this endeavor. In either case, the trend is away from anesthesiologists serving as the primary innovative investigators in this field, and the resulting perception that this specialty is less actively involved in pediatric sedation than other specialists. Indeed, in the last ten years, two premiere medical journals have had reviews on the topic of ‘Pediatric Sedation and Analgesia’ written by emergency medicine physicians (5,6).

In summary, consideration of the evolving literature on pediatric sedation reveals a paradox. Anesthesiologists are still considered critical for oversight of sedation services as defined by important regulatory organizations and medical centers. Conversely, original investigations on the topic of pediatric sedation are

<table>
<thead>
<tr>
<th>Journal</th>
<th>2000</th>
<th>2009</th>
</tr>
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<tr>
<td>Clinical Pediatric Emergency Medicine</td>
<td>22</td>
<td>Gastrointestinal Endoscopy</td>
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<tr>
<td>Gastroenterology</td>
<td>16</td>
<td>Annals of Emergency Medicine</td>
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<tr>
<td>Internal Journal of Pediatric Otorhinolaryngology</td>
<td>14</td>
<td>Journal of Pediatrics</td>
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<tr>
<td>Pediatric Clinics of North America</td>
<td>11</td>
<td>Gastroenterology</td>
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<tr>
<td>Journal of Clinical Anesthesia</td>
<td>10</td>
<td>Pediatrics and Child Health</td>
</tr>
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<td>Journal of PeriAnesthesia Nursing</td>
<td>10</td>
<td>International Journal of Pediatric Otolaryngology</td>
</tr>
<tr>
<td>Anesthesiology Clinics of North America</td>
<td>9</td>
<td>Digestive and Liver Disease</td>
</tr>
<tr>
<td>Emergency Medicine Clinics of North America</td>
<td>9</td>
<td>Annales Francaises d’Anesthesia et de Reanimation</td>
</tr>
<tr>
<td>Journal of the American College of Cardiology</td>
<td>9</td>
<td>European Journal of Pediatric Neurology</td>
</tr>
</tbody>
</table>

Table 1 Top ten journals for publication of pediatric sedation articles according to year. Listing obtained using science direct search key word ‘pediatric sedation’ conducted in June of 2010 during preparation of the manuscript.
increasingly being produced and published by specialists outside of anesthesia. The future role of anesthesiologists in providing leadership in pediatric sedation will hinge on their ability to collaboratively leverage their recognized expertise into new knowledge that improves safety and efficacy of sedation delivery.

NPO and pediatric sedation

The concept of nil per os (NPO) prior to anesthesia for elective surgical procedures has been established for decades. The American Society of Anesthesiologists (ASA) guidelines, based on the best available evidence and expert consensus (2 h for clear liquids, 6 h for light meals etc.), are time honored and have protected millions of patients from possible injury since their inception (7). Regarding sedation, the ASA has historically taken the approach that anyone receiving moderate sedation or deep sedation should be treated similarly to those receiving anesthesia because it is possible that these patients will enter a state where they will have impaired airway protective reflexes. Recently, pediatric sedation literature outside of anesthesiology has questioned the application of these guidelines to pediatric sedation. There is growing skepticism that adherence to these guidelines actually mitigates the risk of aspiration or pulmonary adverse events. Recent publications have raised questions about the basis of these recommendations and the need to adhere to NPO criteria prior to sedation encounters. For example, Roback et al. (8) retrospectively reviewed the charts of approximately 1555 emergency department pediatric sedation encounters. Patients were divided up into cohorts that met ASA NPO criteria prior to sedation and those who did not. The authors looked for evidence of pulmonary adverse events in each case. Their analysis showed no relationship between the incidence of pulmonary adverse events and NPO intervals prior to sedation. They concluded that there was no association. Similarly, Argrawal et al. (9) retrospectively reviewed 905 emergency department sedation encounters. These investigators found 56% of patients in this cohort did not meet ASA NPO criteria. When they examined records for evidence of adverse events, they found no relationship between NPO duration prior to sedation and adverse outcomes. Both of these investigations lack the power to study a relatively rare event such as pulmonary aspiration syndrome that occurs on the order of one in thousands of sedations. The authors use surrogate outcomes such as respiratory adverse events of various kinds to attempt to quantify the association between NPO status and risk to patients.

Based on evidence from studies such as these, The American College of Emergency Physicians (ACEP) published a clinical practice guideline on fasting prior to sedation in 2006 titled ‘Fasting and Emergency Department Procedural Sedation and Analgesia: A Consensus-Based Clinical Practice Advisory’ (10). This advisory begins with an extensive review of the guidelines that have been set forth by the ACEP, AAP, and ASA concerning NPO status and attempts to put them into context when considered with respect to the Emergency Department setting. There is also a discussion of the literature upon which these guidelines have been proposed in the past. This consensus-based clinical advisory proposes that there is scarce literature to document the risk that NPO status poses with respect to sedation complications. The authors suggest that the issue of NPO intervals before sedation needs to be considered in the context of the urgency and duration of the procedure as well as the risk stratification of the patient, nature of food intake, depth and type of sedation targeted. The result is a complex strategy that weighs the issues of NPO time vs urgency of the case, targeted sedation depth, and the duration of the procedure. Figure 1 schematically describes the recommendations that result from this reasoning.

The ACEP recommendations depart from NPO guidelines from other specialties in a number of ways. Most notably, ASA sedation guideline authors have designated a 6- to 8-h NPO interval for solids and have been unwilling to compromise on NPO requirements based on the depth of sedation. The ACEP advisory uses a 3-h NPO cutoff and approves of sedation at specific levels based on the nature of liquid or solid ingested and the urgency of the procedure. Regardless of whether or not this advisory is widely adopted, it is illustrative of changing attitudes toward NPO status held by sedation providers outside of anesthesiology.

Further evidence of a slow erosion in the absolute adherence to NPO guidelines is found in the most influential guidelines for pediatric sedation – the most recent version of the American Academy of Pediatrics (AAP) Guidelines for Monitoring and Management of Pediatric Patients During and After Sedation for Diagnostic and Therapeutic Procedures. These guidelines continue to advocate for adherence to ASA fasting intervals but include language that states “For emergency procedures in children who have not fasted, the risks of sedation and the possibility of aspiration must be balanced against the benefits of performing the procedure promptly…” (11).

The exact importance of prolonged NPO intervals in preventing aspiration and other adverse outcomes...
remains an area of some debate between the various specialists who deliver sedation. Given the rare incidence of major adverse events in pediatric sedation, only very large cohort studies with carefully defined end points will allow evidence-based answers to the question of what are appropriate NPO intervals for pediatric patients undergoing sedation for diagnostic tests and procedures.

**Drug application**

Ketamine was first approved for human use in 1970 and is well established as a drug for sedation of children. It has long been used for procedures that involve significant pain such as burn dressing changes and emergency department procedures (12). The drug provides reliable sedation that is characterized by inducing a cataleptic state with potent analgesia, stable cardiovascular status, and minimal respiratory depression generally described as dissociative sedation or anesthesia. In the last ten years, there have been a remarkable number of studies published on the use of ketamine sedation for children (13–17). In addition to these studies, the American College of Emergency Physicians has published two Clinical Practice Guidelines that advocate for a completely separate categorization of ketamine sedation as ‘Dissociative Sedation’ because of its unique properties (18,19). These guidelines offer specific recommendations for use, contraindications to its use, and separate NPO considerations for ketamine. According to these guidelines, ketamine sedation should be considered completely outside of the usual sedation continuum of minimal, moderate, and deep sedation, as described by the ASA, AAP, or the Joint Commission.

In one recent paper, ‘Predictors of Airway and Respiratory Adverse Events with Ketamine Sedation in the Emergency Department: An Individual-Patient Data Meta-analysis of 8282 Children’ (20), Green et al. used a meta-analysis methodology to delineate the safety and efficacy issues involving ketamine sedation. The authors propose that previous studies of the drug have been too small to give an accurate assessment of factors related to airway emergencies that can occur when this drug is used. The findings in this study included an overall airway/respiratory adverse event rate of 3.9% with higher incidences in children younger than 2 years old (OR 2.0) and older than 13 years old (OR 2.72). High intravenous doses (initial dose >2.5 mg·kg$^{-1}$ or total dose >5 mg·kg$^{-1}$) (OR 2.18) and co-administration of an anticholinergic or benzodiazepine were also noted to have a slightly higher incidence of airway complications. Several common variables that traditionally were thought to add to the risk of ketamine sedation appeared to have no bearing on risk for airway/respiratory adverse events. These
nonrisk-related factors included oropharyngeal procedures, ASA physical status of 3 or greater, and the choice of intravenous (vs intramuscular) route of administration.

In a case control study from Melendez and Bachur (21), 4250 ketamine sedation encounters in a large urban emergency department were evaluated. The authors found a 2.4% incidence of airway events and a 1% incidence of severe adverse events requiring significant intervention. Of the 102 patients who had adverse airway events, 35% required airway repositioning, 7% required CPAP, and 32% required positive pressure ventilation. The data revealed a higher incidence of airway adverse events with IM administration of ketamine. While studies such as this indicate that major adverse events are relatively rare with ketamine, they argue strongly that safe practice with this drug is clearly dependent on the ability to recognize and definitively rescue patients from airway obstruction.

Anesthesiologists recognize that the use of oral ketamine for operative premedication has been around for decades (22). Recently, a single institution study compared oral vs intramuscular ketamine for oncology procedures (23). In this study, a single dose or oral ketamine 10 mg kg$^{-1}$ combined with midazolam and atropine was found to be as effective and equally safe when compared with a single intramuscular 6 mg kg$^{-1}$ ketamine dose combined with IM midazolam and atropine. The authors suggest that the painless administration of oral ketamine may be the preferable route for children undergoing procedures in the future.

Ketamine use also appears to be increasing as a combination drug with propofol for minor painful procedures. Several recent studies tout the ketamine/propofol combination (commonly referred to as Ketofol) to take advantage of the complementary nature of the two medications and maximize effectiveness while minimizing side effects. (i.e., ketamine has minimal respiratory depressant effects compared with propofol, ketamine is emetogenic, and propofol is antiemetic etc.). The ratio of the propofol/ketamine mixture varies from 1:1 to 1:10 in these studies (24-29). The data from these reports, which are primarily prospective and observational, indicate that this drug combination is extremely effective and nausea/vomiting rates are decreased from that of ketamine alone. There is an approximately 1–3% incidence of airway obstruction requiring intervention across these reports. The data are conflicting with regard to the rate of hemodynamic and respiratory complications when this combination is compared with propofol alone. More research is clearly needed to further characterize the nature of the sedation/anesthesia produced by this combination and its safety and usefulness as a strategy for pediatric sedation.

Ketamine has also been to subject of considerable examination with regard to its association with neuronal apoptosis when administered to neonatal rat pups (30,31) and primates (32,33). Other drugs such as inhaled anesthetic agents, barbiturates, and propofol have also been implicated in programmed neuronal cell death when administered to neonatal animal models, but ketamine has been the most carefully studied at this point. Uncertainty remains as to whether or not the doses administered or the developmental status of the animals at the time of exposure actually correlates to human exposure for brief procedures or operations. While the exact relationship between these animal studies and human exposure is uncertain, Dimaggio et al. (34) have reported a possible association between early exposure to anesthesia for hernia repair in children under 3 years of age and subsequent diagnosis of behavioral or learning disorders. Further research is needed to delineate the actual risk infant patients might face from ketamine sedation, but caution in the administration of high doses to young patients is advisable at this point. The outcome of future animal and human studies will determine whether or not ketamine continues its prominent position in pediatric sedation or is abandoned for other options.

**Revolution**

**Adverse event reporting: Quebec guidelines**

A particular problem with the study of risk in sedation/anesthesia outside the operating room is the lack of a clear lexicon of terms that clearly describe adverse events that occur in this practice. Specifically, among the collected community of sedation providers and researchers, there has never been generalized agreement on what constitutes an ‘adverse event’. For instance, is oxygen desaturation to 88% for 30 s an adverse event (it almost always is included as an adverse event in sedation studies)? Should it be given the same general consideration as a severe laryngospasm event that requires intubation to resuscitate the patient? Recently, a group of experts in pediatric sedation were assembled to develop a consensus-based set of recommendations for standardizing procedural sedation and analgesia terminology (35). The goal was to create a uniform reporting mechanism for future studies to facilitate the aggregation and comparison of results. Many of the proposed definitions are similar to those already in use, but the authors have opted for an innovative approach to some of the most contentious
risk-related issues in pediatric sedation. For instance, oxygen desaturation is defined as a drop in oxygen saturation from baseline together with one or more of a list of interventions aimed at improving oxygenation. The interventions range from tactile stimulation to tracheal intubation. The key concept here being that the definition is met only when the specific state of the patient is coupled with an action taken by the provider. Similar operational definitions are proposed for other events such as apnea, airway obstruction, and laryngospasm. A major advantage of this methodology includes the fact that when an event occurs, such as severe airway obstruction, the intervention undertaken to correct the problem before a severe state of desaturation occurs is reported. In the traditional reporting paradigm, where only desaturation below a certain threshold level is recorded, this type of event would be missed or considered only a minor desaturation event.

Standardized definitions have the potential to significantly improve the reporting of sedation adverse events and allow more accurate comparisons of sedation outcomes across the varied specialties that report on pediatric sedation. This is a truly revolutionary concept that a shared reporting structure for adverse events would allow us to understand the results of one study with respect to that of others in the sedation field no matter where it is published. Continued collaborative work on this project is sorely needed to gain input and agreement from a wider range of pediatric sedation practitioners and encourage adoption of a standard terminology for sedation research.

**Sedation drugs**

*Propofol*

No review of the current status of pediatric sedation would be complete without some mention of the status of propofol sedation employed by providers outside of anesthesiology. The use of this drug to provide deep sedation of children by those other than anesthesiologists remains somewhat controversial, but the official recommendations from the ASA have changed significantly in the last three years. In 2006, the ASA adopted the ‘Statement on Granting Privileges to Non-Anesthesiologist Practitioners for Personally Administering Deep Sedation or Supervising Deep Sedation by Individuals Who are not Anesthesia Professionals’ (https://www.asahq.org/For-Members/Standards-Guidelines-and-Statements.aspx). The statement reads ‘Because of the significant risk that patients who receive deep sedation may enter a state of general anesthesia, privileges to administer deep sedation should be granted only to practitioners who are qualified to administer general anesthesia or to appropriately supervised anesthesia professionals.’ As children sedated with propofol for procedures generally meet the definition of deep sedation, this statement effectively represented a recommendation against procedural sedation with propofol (in the pediatric population) by anyone other than anesthesiologists.

In 2010, a new ‘Statement On Granting Privileges for Deep Sedation to Non-Anesthesiologist Sedation Practitioners’ was adopted. (https://www.asahq.org/For-Members/Standards-Guidelines-and-Statements.aspx) This is a detailed statement that recognizes the fact that other medical specialists provide deep sedation. It represents a well-developed rubric for education and training, critical knowledge and skills, monitoring requirements, quality assurance programs, licensure, and performance appraisal that are required to assure effective and safe deep sedation delivery. It attempts to set appropriately high standards for all pediatric sedation practitioners to allow the kind of safety and quality advances that have typified anesthesia progress in the last 40 years.

The ASA statement does not directly refer to deep sedation in children, but there is ample evidence that a significant amount of propofol (deep) sedation is provided by pediatric emergency medicine specialists, intensivists, and hospitalists. Over 100 studies have been published in the last five years describing the use of propofol sedation for procedures outside the operating room in children of which we can only cite several (36-40). Most of these studies evaluate small numbers of patients undergoing specific procedures in very controlled settings. One larger series was reported by Vespasiano et al. (41). This study prospectively evaluated 7304 propofol sedation encounters in a children’s hospital ICU sedation service. The authors detail a high success rate for propofol along with a low rate of adverse events and interventions (laryngospasm 0.27%, regurgitation with aspiration 0.01%, cardiac arrest 0%, intubation 0.03%). These investigators used patient history of airway problems (stridor, obstructive sleep apnea, craniofacial anomaly) to separate patients into low- vs high-risk classes. Not surprisingly, they found that patients with high-risk airway profiles were much more likely to have oxygen desaturation events (13.1% vs 4.3%) or require nasal airways (13.9% vs 1.2%) during sedation. They conclude that propofol has ‘an acceptable safety profile for deep sedation when used in the context of a program with critical care physicians, specifically trained nurses, and anesthesiology oversight.’

A large multispecialty database study has also attempted to address rate and nature of adverse events...
involving sedation/anesthesia with propofol (42). This study was produced by the Pediatric Sedation Research Consortium, a collaborative group of 37 institutions that share information on sedation practice. The study looked at adverse events and efficacy of propofol-based sedation as delivered by the multi-specialty group of providers participating in the consortium. Nearly 50,000 sedation encounters using propofol were evaluated. The results were remarkable for a low rate of serious adverse events (Table 2).

There were no deaths, two codes and six aspiration events were reported. An extremely high efficacy rate of over 99% successful sedation accomplishment was also documented. As with the prior study, the authors gathered information on airway interventions and found that 1 in 65 of the sedation encounters required an airway intervention such as a chin lift, jaw thrust, airway insertion, or positive pressure ventilation. The authors suggest that their data does not prove that propofol sedation is ‘safe’. Rather, they suggest that propofol sedation is associated with serious adverse events.

**Table 2** Adverse events during propofol anaesthesia (N = 49,836) approximately rates per 10,000

<table>
<thead>
<tr>
<th>Complication</th>
<th>Number</th>
<th>Rate</th>
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<tbody>
<tr>
<td>Inadequate anesthesia</td>
<td>394</td>
<td>85.0</td>
<td>76.8, 93.8</td>
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<tr>
<td>Airway obstruction</td>
<td>432</td>
<td>93.2</td>
<td>84.6, 102.3</td>
</tr>
<tr>
<td>Allergic reaction</td>
<td>14</td>
<td>3.0</td>
<td>1.7, 5.1</td>
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<tr>
<td>Apnea</td>
<td>143</td>
<td>30.8</td>
<td>26.0, 36.3</td>
</tr>
<tr>
<td>Aspiration</td>
<td>4</td>
<td>0.9</td>
<td>0.2, 2.2</td>
</tr>
<tr>
<td>Cardiac arrest</td>
<td>2</td>
<td>0.4</td>
<td>0.1, 1.6</td>
</tr>
<tr>
<td>Cough (interrupts procedure)</td>
<td>356</td>
<td>76.8</td>
<td>69.0, 85.2</td>
</tr>
<tr>
<td>Death</td>
<td>0</td>
<td>0.0</td>
<td>0.0, 0.8</td>
</tr>
<tr>
<td>Desaturation (&lt;90% &gt;30 s)</td>
<td>716</td>
<td>154.4</td>
<td>143.4, 166.1</td>
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<tr>
<td>Emergency anesthesia consult*</td>
<td>7</td>
<td>1.5</td>
<td>0.6, 3.1</td>
</tr>
<tr>
<td>Hypothermia</td>
<td>6</td>
<td>1.3</td>
<td>0.5, 2.8</td>
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<tr>
<td>IV complications</td>
<td>113</td>
<td>24.4</td>
<td>20.1, 29.3</td>
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<tr>
<td>Laryngospasm</td>
<td>96</td>
<td>20.7</td>
<td>16.8, 25.3</td>
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<tr>
<td>Myoclonus (interrupts procedure)</td>
<td>11</td>
<td>2.4</td>
<td>1.2, 4.2</td>
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<tr>
<td>Prolonged recovery</td>
<td>42</td>
<td>9.1</td>
<td>6.5, 12.2</td>
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<tr>
<td>Prolonged sedation</td>
<td>30</td>
<td>6.5</td>
<td>4.4, 9.2</td>
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<tr>
<td>Secretions (require suction and interrupt procedure)</td>
<td>341</td>
<td>73.6</td>
<td>66.0, 81.8</td>
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<tr>
<td>Seizure – interrupts procedure</td>
<td>11</td>
<td>2.4</td>
<td>1.2, 4.2</td>
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<tr>
<td>Stridor – interrupts procedure</td>
<td>50</td>
<td>10.8</td>
<td>8.0, 14.2</td>
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<tr>
<td>Change in HR, BP, RR of &gt; or &lt;30%</td>
<td>282</td>
<td>60.8</td>
<td>53.9, 68.3</td>
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<tr>
<td>Unintended deep sedation</td>
<td>4</td>
<td>0.9</td>
<td>0.2, 2.2</td>
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<tr>
<td>Unexpected admission</td>
<td>33</td>
<td>7.1</td>
<td>4.9, 10.0</td>
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<tr>
<td>Reversal agent required</td>
<td>2</td>
<td>0.4</td>
<td>0.1, 1.6</td>
</tr>
<tr>
<td>Vomiting during sedation</td>
<td>49</td>
<td>10.6</td>
<td>7.8, 14.0</td>
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<tr>
<td>Wheezing – interrupts procedure</td>
<td>44</td>
<td>9.5</td>
<td>6.9, 12.7</td>
</tr>
</tbody>
</table>

*Emergency airway consultation – does not apply to cases delivered by anesthesiologists [from Cravero et al. (42) with permission].

(as practiced by the members of this consortium with good protocols and appropriate oversight) excellent efficacy and a good safety record are possible.

The limitations of this kind of data analysis are clear. There is nonuniformity of technique, providers, patient selection etc., which makes direct comparison of sedation performance impossible. This kind of study does, however, give a general description of the nature of propofol use in a wide range of institutions as well as the events that are associated with this practice. What is clear from the current literature on this topic is that the propofol ‘revolution’ is well underway. A large number and variety of sedation providers are utilizing this drug for sedation of children and it deserves continued study and surveillance.

**Dexmedetomidine**

Since its approval for ICU sedation in 1999, the alpha-2 agonist dexmedetomidine (DEX) has also been used for sedation outside the operating room. Its use in children for procedural sedation, particularly in diagnostic radiology, is well reported and continues to increase (43). Its use may well change the very nature of sedation delivery, specifically involving sedation providers outside of anesthesia who are limited in using other medications such as propofol. When compared with older sedatives such as pentobarbital, it offers clear advantages in terms of rapidity of emergence and lower incidence of emergence delirium and agitation (44). The safety and efficacy of this drug for sedation has been the focus of several recent investigations (45–47). Two papers from Mason et al. have shed some light on the issues involved with the use of DEX for radiological procedures. The first of these studies used an observational database to evaluate the safety and effectiveness of this drug as using three different dosing regimens – all of which were considerably higher than the manufacturers’ recommended dose of this drug for sedation (48). In this study, the authors progressively increased the dose of DEX to optimize performance of the drug. The final (highest) dose regimen included a bolus of 3 μg·kg⁻¹ over 10 min followed by a 2–μg·kg⁻¹·h⁻¹ infusion. A total of 747 consecutive sedations with DEX were evaluated. Their data indicated that the effectiveness of sedation was significantly improved (from 91.8% to 97.6%) when the highest dose was employed. Respiratory depression was not an issue, but there was a significant incidence of bradycardia. In the entire cohort, 16.1% had heart rates that fell below age-specific norms; however, only 4% of patients had heart rates that fell >20% below the lower limits of normal for age. In several cases, heart rates fell to <60 b·min⁻¹ for...
patients < 1 year of age. In spite of this finding, oxygen saturations remained > 95% and the blood pressure remained in the normal range. No treatment was administered. There was no sequelae from the bradycardia reported in any of these patients. The authors warn that providers need to be ready for this side effect with DEX at these doses. It remains unclear if this level of bradycardia is associated with significant cardiopulmonary insufficiency under this particular set of circumstances.

Mason et al. (49) also reported an exaggerated hypertensive response to glycopyrrolate therapy for bradycardia associated with high-dose DEX. This report consists of three case descriptions of patients who experience bradycardia while receiving high-dose DEX for radiology diagnostic procedures. In each case, 5 μg·kg\(^{-1}\) of glycopyrrolate was administered resulting in resolution of the bradycardia and significant increases in blood pressure with reported mean arterial pressures increasing to well over 100 mmHg from baselines in the 60 mmHg range. The authors theorize that this increase is because of increased heart rate in the face of increased systemic vascular resistance from α receptor occupation in the peripheral blood vessels. They advise that treatment of bradycardia in the presence of DEX with glycopyrrolate should be avoided.

To further evaluate bradycardia associated with DEX, Hammer et al. (50) studied 12 children undergoing electrophysiology studies while under standard dexmedetomidine infusions. Sinus node and atrio-ventricular node function was significantly depressed in these patients. The authors recommend against the use of this agent for electrophysiology studies or in children with a risk of bradycardia or heart block.

Several other studies have compared the effectiveness and safety of DEX for sedation outside the OR with other drug options (46,51). Heard et al. (52) compared a combination of DEX/midazolam with propofol for MRI imaging. Doses employed for DEX were considerably lower (0.5 μg·kg\(^{-1}\) bolus followed by 0.5–2 μg·kg\(^{-1}\)·h\(^{-1}\) infusion) than those used by Mason et al. The 40 patients randomized to the two drug regimens were found to have similar respiratory indices. Heart rates were lower, and blood pressures were higher in the DEX cohort – no profound bradycardia was noted. The only difference recorded between the groups was a longer time to awakening in the DEX/midazolam cohort.

Dexmedetomidine sedation continues to be the subject of active investigation. Its use is still relatively new and much work remains to define its pharmacodynamics and cardiovascular impact in children. In spite of this, its lack of respiratory depression combined with favorable emergence characteristics ensures that it will grow in use and perhaps revolutionize radiological sedation where anesthesiologists (or other highly skilled airway management experts) are not available to provide direct sedation services.

**Human patient simulation**

Human patient simulation (HPS) continues to grow and will doubtless fundamentally change the nature of medical education in the future. Anesthesiologists have been at the forefront of this new educational tool application. HPS has the advantage of offering a controlled environment in which to introduce learners to clinical situations, including those that are relatively infrequent. With modern HPS technology, simulated environments can closely resemble those of actual care. In addition, centers which focus on teaching with HPS videotape scenarios as students work through them. They allow detailed analysis and feedback on performance that is not possible when trainees learn during the course of regular patient care. Finally, HPS training has the advantage of not placing patients at risk while teaching new techniques or procedures to learners (53).

Adult sedation literature has documented a role for HPS in training for sedation providers (54), while the literature on the use of HPS related to pediatric sedation is just now beginning to join this vanguard. Shavit et al. (55) studied the use of HPS in training pediatric sedation providers and demonstrated improved sedation safety performance in a cohort of pediatrician sedation providers who had trained with HPS when compared with a cohort of providers who had not received simulation training. While the study was small, it is the first to attempt to validate this form of training and its contribution of sedation provider skills. Simulation can also be used to document physiological responses in human systems through the use of algorithm-driven simulator physiology. As an example, Keidan et al. employed HPS to document the effect of supplemental oxygen on the ability of pulse oximetry to detect apnea. This straightforward study confirmed the concept that patients on oxygen will be delayed in experiencing oxygen desaturation during apnea when compared with patients not on oxygen (56). HPS can also be utilized to test rescue systems. Blike et al. (57) published work on the use of HPS to detect latent problems in sedation rescue systems within a given sedation system. In this study, a simulator was used as a ‘test patient’ for several sedation systems and response to a standardized emergent event...
was documented. The results showed significant differences in the ability of sedation providers to rescue a patient from a difficult sedation mishap. The authors argue that only through realistic real-time testing can medical systems understand and improve their response to rare life-threatening events.

While it is clearly too early to report that HPS is revolutionizing pediatric sedation, it deserves mention as a technology with the potential to radically change the way in which we train, credential, and test the readiness of sedation providers and systems.

Conclusion
The field of pediatric sedation continues to be one of ongoing change and progress. There is no question that leadership in this area of medicine will continue to be shared between pediatric specialties and is not the domain of anesthesiologists alone. In addition, an effort to unify a set of definitions for adverse events, which could allow those who study and research sedation to easily compare work and outcomes, is underway. Finally, there appears to be a new paradigm for drug utilization in pediatric sedation. Older drugs such as ketamine and newer sedatives such as propofol and dexmedetomidine are changing the face of sedation practice. Older less potent medications appear to be giving way to these more effective alternatives. Continued vigilance and a demand for careful outcome analysis will be required to be sure these changes in sedation practice and science ultimately benefit our patients.

References
25 Slavik VC, Zol PJ. Combination ketamine and propofol for procedural sedation and


