Pediatric Sedation Outside the Operating Room

Mario Patino, MD
Paul Samuels, MD
Mohamed Mahmoud, MD
Cincinnati Children's Hospital Medical Center
University of Cincinnati
Cincinnati, Ohio

Objectives

1. Recognize and identify the continuum of depth of sedation.
2. Discuss the complexity of the current practice of pediatric procedural sedation.
3. Outline the principles of creating a sedation plan in children.
4. Review pharmacological principles of the most common sedatives.

The practice of medicine is evolving as health care is impacted by technological innovation, which has allowed the development of multiple invasive and noninvasive pediatric procedures and imaging modalities. This clinical demand has resulted in tremendous growth in procedural sedation (PS) in children.[1] PS is defined as the use of sedative, analgesic, or dissociative drugs to provide anxiolysis, analgesia, and sedation, during diagnostic, painful, or unpleasant procedures.[2] Many of these procedures occur outside the traditional operating room setting, and range from painless imaging studies to uncomfortable invasive interventions. This chapter describes the challenges of pediatric PS outside the operating room and reviews the knowledge and technical skills required for safe and effective care of children in this clinical setting.

Pediatric Sedation Policies, Guidelines, and Required Professional Skills

Pediatric PS is provided by a broad range of practitioners including anesthesiologists, intensivists, pediatricians, dentists, emergency physicians,

Reprints: Mohamed Mahmoud, MD, Department of Anesthesiology and Pediatrics, Cincinnati Children's Hospital Medical Center, 3333 Burnet Ave, Cincinnati, OH 45229. E-mail: mohamed.mahmoud@cchmc.org

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gasroentrologists, and podiatrists. This practitioner heterogeniety has resulted in a complex healthcare landscape in which little consensus exists among providers regarding who should deliver this service, and how it should be delivered.[3,4] The practice variation has induced a call for more consistent guidelines in an effort to improve patient safety and sedation efficiency.[5]

Anesthesiologists have been at the forefront of safety guideline development for PS. In 1983, the first sedation guidelines were published in response to 3 deaths in a dental office.[6] Since then, many organizations including the American Society of Anesthesiology (ASA), the American Academy of Pediatrics (AAP), and the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) have created standards for institutional policy development in pediatric PS. In 2004, JCAHO published their Comprehensive Accreditation Manual for Hospitals, intended to set standards for sedation and anesthesia care for patients in all clinical settings. The JCAHO Manual was updated in 2007, with a new mandate that individuals administering moderate or deep sedation be qualified and credentialed to manage all levels of sedation. In 2011, the Center for Medicaid and Medicare Services (CMS) published their guidelines that are consistent with the ASA's qualification requirements for deep sedation in which this practice is not restricted to anesthesiologists.[7–9] Under these guidelines, Registered Nurses are no longer qualified to administer deep sedation. The sedation provider must be a physician, nurse anesthetist, or anesthesia assistant. Any qualified specialist can play the main role in privileging programs for sedation. Currently at most institutions, the director of anesthesia services determines the proficiency and competency. In general, the required skills and competencies include performance of a preprocedural risk analysis, knowledge and experience of applied sedatives, implementation of the necessary monitoring and surveillance, identification and interpretation of sedation levels, and recognition and management of any unwanted adverse effects, particularly hypoventilation and airway obstruction.

Currently, there is a lack of universally accepted credentialing process for providers of pediatric sedation. Many institutions, including our own, require certification in Pediatric Advanced Life Support and Basic Life Support, as well as satisfactory performance on an examination after an online review of sedation educational content. Some centers recommend simulation-based training for nonanesthesiologists.[10] The quality of training becomes particularly important in remote areas of the hospital or in the office setting where assistance is difficult to provide in the event of a life-threatening emergency. We consider that equal safety precautions and requisite technical skills should be in place when any type of PS greater than mild sedation is provided; irrespective of which sedative is chosen. Consequently, it is

Table 1. *Recommended Specific Additional Skills and Competence for Achieving Optimal Safety During Moderate and Deep Sedation in Children*

N	Recommendations
(1)	In order to guarantee optimal levels of safety and effectiveness during a PS involving (a possibility of) moderate-to-deep sedation, the PS must be carried out by a separate professional that is not involved in the actual procedure
(2)	During a PS involving (a possibility of) moderate or deep sedation and during the subsequent recovery phase, a professional must be present with at least the following additional competence and skills: (1) The ability to assess and interpret the sedation depth (2) The ability to guarantee the necessary monitoring of vital parameters, including capnography, and being able to appraise and interpret the monitored information (3) Having acquired the necessary knowledge during a specialist course and by means of refresher courses and ability to manage the following techniques at APLS level: (3.1) Techniques intended to guarantee an open airway, including skills to manage larynx spasm and to use laryngeal mask airways (3.2) Techniques to administer mask/bag ventilation (3.3) The use of antagonists (3.4) Heart massage techniques

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APLS indicates advanced pediatric life support; PS, procedural sedation.

wise to formulate separate recommendations regarding professional skills and competence for mild sedation on one hand and for moderate to deep sedation on the other hand (Tables 1, 2).[11]

■ Sedation Levels and Available Pediatric Sedation Scales

The Joint Commission, the ASA, and the AAP have recently revised their definitions of the levels of PS. The 4 levels of sedation shown in Table 3 are now minimal, moderate, deep, and general.[5,12] Although sedation levels are described as discrete entities, it must be recognized that sedation exists on a dynamic continuum, and that levels of sedation can change rapidly. This dynamic quality of sedation leads to the principle that the individual performing sedation must be capable of rescuing a patient from a depth of general anesthesia, implying that the clinician is skilled in advanced airway management and the treatment of cardiorespiratory compromise.

Sedation scales are scoring systems that describe the level of consciousness. Unfortunately, there is no ideal sedation scale available in pediatrics. However, there are number of validated sedation scales currently utilized to allow practitioners to intervene, instead of having to rescue the patient from complications related to increasing depth of

Table 2. *Specific Additional Skills and Competence for Achieving Optimal Safety During Mild Sedation/Anxiolysis in Children*

N	Recommendations
(1)	During a PS involving mild sedation and during the subsequent recovery phase, a professional must be present with the at least the following additional competence and skills: (1) The ability to assess and interpret the sedation depth (2) The ability to maintain continuous verbal contact with the patient in the absence of any other form of monitoring (3) Having acquired the necessary knowledge through a specialist course and by means of refresher courses and the ability to manage the following techniques at BLS level: (3.1) Techniques intended to guarantee an open airway (3.2) Techniques to administer mask/bag ventilation

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BLS indicates basic life support; PS, procedural sedation.

sedation. The most commonly used pediatric sedation scales include Ramsay Scale,[13] the Observer's Assessment of Alertness/Sedation Scale,[14] the COMFORT Scale,[15] University of Michigan Sedation Scale,[16] and Dartmouth Operative Conditions Scale.[17]

Defining sedation depth based on responsiveness is inherently limited, as the implicit need to stimulate the patient in order to assess the sedation level. Moreover, this approach is challenged in circumstances when children are unable to respond appropriately, such as with the hearing impaired, the neurologically or developmentally compromised, or those who are preverbal or who speak a foreign language. Recently, Green and Mason[18] advocate for a reformulation of the assessment of

Table 3. *ASA Definitions of General Anesthesia and Levels of Sedation/Analgesia*

	Minimal Sedation (Anxiolysis)	Moderate Sedation/ Analgesia	Deep Sedation/ Analgesia	General Anesthesia
Responsiveness	Normal response to verbal stimulation	Purposeful response to verbal or tactile stimulation	Purposeful response after repeated or painful stimulation	Unarousable, even w/painful stimulus
Airway	Unaffected	No intervention required	Intervention may be required	Intervention often required
Spontaneous ventilation	Unaffected	Adequate	May be inadequate	Frequently inadequate
Cardiovascular function	Unaffected	Usually maintained	Usually maintained	May be impaired

ASA indicates the American Society of Anesthesiology.

sedation depth from the subjective assessment of responsiveness toward objective vital sign monitoring, for example, pulse oximetry, impedance respiratory rate monitoring, automated noninvasive blood pressure measurement, and ventilation monitoring with capnography. This tool, known as the Objective Risk Assessment Tool for Sedation, would be used in conjunction with comfort assessment for sedation, which reflects the degree of comfort.[19]

■ Formulating a Plan to Sedate a Child Outside the Operating Room

Safe and effective PS begins with a careful presedation evaluation focusing on the underlying medical conditions. The age and maturity of the patient and the nature of the procedure dictate the required sedation depth. Therefore, the formulation of a sedation plan depends on the patient's age, comorbidities, allergies, and the requirements of the study or procedure. Specific institutional practices influence the selection of an agent. Some interventions are performed with minimal alteration in consciousness. Other procedures are better served under deeper levels of sedation or general anesthesia. In general, young children do not tolerate discomfort or immobility. Nonstimulating procedures, when lengthy, often require sedation as well. The sedation provider must ask about previous sedation or anesthesia, as a history of a failed sedation or other complications will undoubtedly influence the sedation plan.

It is critical to differentiate children for whom sedation can be provided by a nonanesthesiologist and children who require anesthesiology management. Every Department of Anesthesiology must assigned an anesthesiologist with expertise on PS to whom nonanesthesiologists may direct questions regarding sedation planning. This leader should be familiar with institutional sedation guidelines, the broad requirements for PS, and the clinical and systemic limitations within the institution that impact clinical care.

Patients receiving moderate or deep sedation should abide by the same NPO guidelines as patients receiving general anesthesia, as sedation levels may rapidly change with impairment of airway reflexes. The ASA guidelines for fasting are 8 hours from the intake of a meal that includes fried or fatty foods, 6 hours after the patient receives infant formula or a light meal, 4 hours after breast milk, and 2 hours after clear liquids.[20] It is important to recognize that these guidelines are based on consensus opinion rather than evidence. Furthermore, the guidelines acknowledge that there is "insufficient" evidence to address the relationship between the preoperative fasting period and aspiration risk. We also lack guidance regarding specific fasting recommendations for emergency procedures.[21] When practitioners formulate a plan for sedation 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 with an unprotected airway. The American College of Emergency Physicians (ACEP) advisory includes a minimum of 3 hours of fasting and approves of sedation at specific levels based on the nature of liquid or solid ingested and the urgency of the procedure.[21] Aspiration was found to be very rare among patients sedated in an emergency room setting for procedures despite not being appropriately fasted.[22] In another study, 2 aspiration events occurred in a population of over 16,000 children sedated for radiologic procedures.[23] Approximately two thirds of aspiration occurs during manipulations of the airway (endotracheal tube placement and removal). Although most patients undergoing general anesthesia have cuffed endotracheal tubes in place, aspiration can occur despite such protection.[24] The low incidence of aspiration during sedation has been attributed to maintenance of protective airway reflexes. However, rapid progression from mild sedation or analgesia to general anesthesia may occur.[25]

The management of children who require oral contrast for computed tomography (CT) scan is controversial. Our institutional protocol begins contrast administration 2 hours and ends 1 hour before PS. The challenge lies in balancing technical factors governing the image quality of the study with safety concerns related to sedating a child with a potentially full stomach for an elective CT. There is considerable variation in sedation/anesthesia practices and in airway management techniques. Currently, there is no consensus among institutions. Different anesthetic plans include rapid sequence induction of general anesthesia with tracheal intubation, deep sedation without airway protection, oral contrast given 2 hours before the study or administered through an oral gastric tube after placement of an endotracheal tube.[26,27]

■ Monitoring Patients During and After PS

The ASA has established guidelines for monitoring during moderate and deep sedation.[28] These guidelines represent recommendations rather than standards of practice. Many of the principles of basic physiological monitoring during general anesthesia apply during moderate and deep sedation including the presence of qualified personnel, hemodynamic monitoring with electrocardiography (in selected patients during moderate sedation), noninvasive blood pressure measurements at least every 5 minutes (unless such monitoring interferes with the sedation level), pulse oximetry and continuous monitoring of patient's ventilation by clinical evaluation, or in deep sedation with exhaled carbon dioxide (end-tidal CO_2). During moderate sedation, end-tidal CO_2 monitoring is recommended when conditions limit the ability to observe the patient. Respiratory rate

monitoring with transthoracic impedance is considered inaccurate and unreliable. Considering the risk of excessive sedation, the level of consciousness must be regularly assessed. However, this recommendation has limitations during the sedation of children when stimulation impedes the completion of a diagnostic procedure. Documentation of recorded monitored parameters during PS is obligatory, beginning before sedation is administered and ending at the time of discharge.

Adapting these guidelines to every clinical setting is a challenge, particularly when the environment is designed for the proceduralist rather than the sedation provider. Sedation providers commonly face many safety issues, including limited patient access, poor lighting, and equipment that cannot be used in every environment. In these settings, reliable and accurate physiological monitoring is critical for patient safety. Anesthesiologists should assist in the early design phases of procedural and diagnostic rooms so that appropriate sedation resources are in place.[29]

Sedation for radiotherapy and magnetic resonance imaging (MRI) is associated with unique monitoring challenges. Sedation providers are often physically isolated from patients. In this setting, remote video monitoring provides visualization the patient's chest wall movement. Because of risk of burns when applying standard pulse oximeters and EKG leads[30] in the MRI suit, "MRI compatible" monitors based on fiberoptic technology for signal acquisition should be used. These technologies promote more accurate and reliable monitoring due to their resistance to artifact.

■ Review of Medications Used for Pediatric Sedation

The following section reviews the most commonly used medications presently administered for pediatric sedation. See Table 4 for dose recommendations and specific considerations.

Barbiturates

It is useful as a single agent for noninvasive procedures providing a deep sedation level through stimulation of $GABA_A$ receptors. Pentobarbital, the most common barbiturate used for PS to children, can be administered orally, intramuscularly, rectally, and intravenously. Intravenous route produces the most predictable sedation in children. In infants, oral pentobarbital is highly effective with slower onset, less oxygen desaturation, and similar time to discharge readiness when compared with intravenous pentobarbital.[31] Oral pentobarbital has a mean time to sedate of 19 ± 14 minutes, a sedation length of 81 ± 34 minutes, and a discharge time of 100 ± 35 minutes.[32] It preserves respiratory and cardiovascular function with minimal respiratory depression. Unsuccessful sedation is as low as 0.3%. Rare side effects include paradoxical excitation, prolonged

Table 4. *Recommended Doses of Sedatives*

Pharmacological Agent	Doses	Special Considerations
Pentobarbital	PO: 2-6 mg/kg IV: 3 mg/kg. Up to 7 mg/kg total	Increase PO dose up to 9 mg/kg on patients already on barbiturate therapy
Methohexital	IV: Initial: 0.5 mg/kg. Repeat on increments of 0.5 mg/kg to a maximum dose of 2 mg/kg. Rectal: 20-35 mg/kg IM: 5-10 mg/kg/dose	Alkaline medication, incompatible with acids (atropine, succinylcholine), single IV administration has a duration of 7-10 min
Thiopental	Rectal 5-10 mk/kg IV: 2-3 mg/kg	Potent, can lead to apnea, risk in asthmatic patients of inducing bronchospasm
Chloral hydrate	Oral or rectal: 25-100 mg/kg	Associated with prolonged residual sedation that could last up to 4-8 h
Propofol	Bolus: 1-2 mg/kg Continuous: 150-250 mcg/kg/min	Younger patients need higher rate than older children
Fospropofol	Bolus 6.5 mg/kg Supplemental doses given no less than every 4 min	Not available studies in infants, children, and adolescents
Dexmedetomidine	Load: 2-3 mcg/kg over 10 min Continuous: 1.5-2 mcg/kg/h	Glycopyrrolate administration to treat bradycardia can result in severe hypertension
Midazolam	Oral: 0.25-1 mg/kg IV: 0.05-0.1 mg/kg	More commonly used as an adjunct
Ketamine	IV bolus: 0.25-1 mg/kg Continuous: 20-35 mcg/kg/min	Incidence of behavioral reactions in children 1%-4%
Propofol-ketamine ("Ketofol")	1:1 mixture bolus: 0.5-0.75 mg/kg Continuous: 10:1-2 mixture: 75-100 mcg/kg of propofol	No standard doses. Multiple regimens used in the literature
Fentanyl	0.5-2 mcg/kg	Commonly used as adjunct with the administration of pentobarbital

IM indicates intramuscular; IV, intravenous; PO, oral.

sedation, and transient oxygen desaturation. It has a long half-life of 24 hours; consequently, parents must be aware of the potential for prolonged somnolence and irritability. The intravenous preparation of pentobarbital contains 40% propylene glycol, which can cause metabolic acidosis, seizures, and renal failure especially with larger doses and intravenous continuous infusion. Pentobarbital induces CYP3A4; medications metabolized by this pathway, such as calcium channel blockers, can lose their effectiveness. Thiopental and methohexital have been used safely for radiographic sedation in children.[33] Methohexital has a shorter half-life than thiopental

and should be avoided in patients with temporal lobe epilepsy due to its potential to cause seizures.[34]

Benzodiazepines

It is used as an anxiolytic with minimal cardiorespiratory depression when not coadministered with other sedatives. Midazolam is the most commonly used benzodiazepine due to its short (2.5 h) half-life. Benzodiazepines are rarely used as the sole sedation agent as it lacks sufficient potency to result in deep sedation unless used at very high doses. Different routes of administration includes oral, intranasal, intramuscular, or intravenous.

Propofol

It is a potent hypnotic agent used as an induction agent and sedative in children. It should be used with caution as it may result in upper airway obstruction and apnea. Its administration requires continuous monitoring and providers skilled in advanced airway management. The provider using propofol should never be involved with the diagnostic or therapeutic procedure, as a loss of airway control demands immediate intervention. Propofol administration by nonanesthesiologists has generated tremendous controversy. The ASA guidelines specifically state that personnel qualified to provide general anesthesia should only administer this medication.

Fospropofol

It is a water-soluble (rather than a lipid emulsion like propofol) prodrug that is converted to propofol by hydroxylation. It is an aqueous solution with some advantages over propofol including lower potential for contamination and decreased pain on injection. Its onset of action is slower, and its duration is longer than propofol. This drug is not yet approved for patients younger than 18 years of age.

Dexmedetomidine (DEX)

It is a highly selective α2-adrenoceptor agonist with sedative, anxiolytic, and limited analgesic effects. Inhibition of sympathetic outflow from the locus ceruleus in the brainstem results in sedation and anxiolysis. It has a half-life of 2 to 3 hours, and its clearance decreases with hepatic impairment. DEX is available for intravenous administration, although intramuscular, intranasal, subcutaneous, and epidural administration has been reported. Although it is not FDA approved in children, it is widely used as an adjunct to pediatric anesthesia and pediatric sedative in many settings. In contrast to other sedative

agents, DEX has been shown to have sedative properties that mimic natural sleep, without significant respiratory depression.[35] Electroencephalograms in children under DEX sedation resemble those during nonrapid eye movement sleep.[36] Even in relatively high doses, DEX has little effect on airway caliber in children,[37] making this agent attractive in children with obstructive sleep apnea.[38] DEX has been used as the sole sedative agent providing reliable, effective, and hemodynically stable sedation in a variety of clinical settings including cardiac catheterization suite, radiology, and in intensive care. We administer DEX as an intravenous bolus of 1 to 3 μg/kg over 10 minutes followed by infusion rates of 1 to 3 μg/kg/h when used as the sole sedative. Transient hypertension and bradycardia has been reported during bolus administration.[38,39] DEX administration should proceed through an initial loading infusion, followed by a maintenance infusion, rather than rapid intravenous bolus to avoid hypertension and reflex bradycardia. Hypotension and bradycardia are the most common adverse reactions associated with the use of DEX. Exaggerated hypertension has been reported after the administration of glycopyrrolate to treat bradycardia.[40]

Ketamine

It is a phencyclidine derivative inducing a dissociative state by blocking communication pathways between the thalamus and the limbic system. It has analgesic properties with minimal cardiovascular depression, with the exception of the catecholamine-depleted patients. It is frequently administered during painful procedures such as dressing changes in burn patients and closed reduction of fractures in children. Unpleasant experiences associated with the administration of ketamine to children including hallucinations, agitation, and nightmares occur in 1% to 4%.[41] These behavioral reactions are not different from young to older children.[41] A meta-analysis of >8000 PS with ketamine administered by emergency physicians found a 3.9% incidence of a respiratory event with highest risk on children younger than 2 years and older than 13 years, the use of high intravenous doses (initial dose >2.5 mg/kg or total dose > 5 mg/kg), and the administration of anticholinergics.[42] Despite these results, the adverse events of ketamine are quite different than other agents, with higher incidence of hypertension, nausea, and vomiting and lower risk of respiratory events.

Opioids

These are commonly used during invasive procedures, although rarely for diagnostic imaging except as a rescue drug in cases of failed sedation or when dose limits of other sedatives have been exceeded. Fentanyl is commonly used in this setting due to its rapid onset and

short half-life. Caution should be exercised when opiates are combined with other sedatives as the risk of respiratory depression is substantial. Naloxone, an opiate antagonist, should be readily available when opiates are used. Naloxone administration can be associated hypertension, tachycardia, pulmonary edema, and uncontrolled pain. The administration of opioids during PS increases the incidence of nausea, vomiting, and pruritus in the recovery period.

Chloral Hydrate

It is given by oral or rectal route. Its highly variable absorption can result in unpredictable onset, prolonged sedation, and persistent residual somnolence. An oral dose of 50 mg/kg in infants is as effective as oral pentobarbital with regard to onset of sedation and time to discharge. Desaturation is more common after chloral hydrate administration than with pentobarbital.[43]

Nitrous Oxide

It is commonly used during PS in the emergency department as well as during dental procedures. It has been used in concentrations from 30% to 70%. Sporadic report of seizures was reported during dental procedures.[44]

The side effects of sedatives are dose dependent. Therefore, combining medications with different pharmacokinetic and pharmacodynamic profiles have the possible advantages of increasing efficacy and decreasing the side effects. One of these coadministered sedatives is propofol and ketamine. This combination has the potential of decreasing the risk of respiratory depression and hypotension with propofol, and decreasing the incidence of hallucinations, agitation, nightmares, nausea, and vomiting with the administration of ketamine. A prospective randomized controlled study in pediatric patients undergoing cardiac catheterization found that at a propofol:ketamine ratio of 10:2 (10 mg/mL of propofol and 2 mg/mL of ketamine) provides better hemodynamic profile without affecting the recovery time.[45] Similar findings were found in a prospective study using higher concentrations of ketamine (propofol:ketamine ratio 10:5) on pediatric patients undergoing cardiac catheterization.[46] In pediatric burn patients, propofol ketamine infusions have also found more effective than propofol fentanyl infusion for dressing changes.[47] Multiple studies have been done in the emergency room setting, comparing the administration of propofol ketamine versus the administration of ketamine both as a bolus. All of them include small number of patients and have shown conflicting results and its role is not defined.[48] During monitorized anesthetic care in adults, a study using 3 different mixtures of propofol and ketamine (propofol: ketamine 10:1, 10:2, and 10:3) showed that ketamine provides analgesia and reduces the administration of supplementation with opioids. However, in the

largest ketamine group dose, there was an increase incidence of nausea, vomiting, psychomimetic effects, and prolonged discharge times.[49] In conclusion, the administration of propofol and ketamine on continuous infusion have shown clear advantages on children with congenital or acquired heart disease especially on those with labile hemodynamics and in burned children. However, there is no support of using this combination for routine sedation in children without cardiovascular disease. Current studies use different regimens of propofol and ketamine with different end-points and further studies in children are necessary to better evaluate the efficacy of propofol-ketamine given simultaneously.

Adverse Sedation Events and Risks Related to Pediatric Sedation

The Pediatric Sedation Research Consortium is a group of 37 institutions that have combined their sedation data to generate powerful insights into adverse events during PS. The consortium has pooled data from highly organized sedation services with robust sedation competencies. Their analysis of >30,000 PS provided by anesthesiologists, intensivists, emergency physicians, and hospitalists during therapeutic or diagnostic studies with the use of different sedatives (50% propofol) outside the operating room demonstrated that major complications were uncommon, and when they did occur were benign in nature when managed by skilled personnel. However, the incidence of airway intervention (including need for an oral airway, positive pressure ventilation, or intubation) was 1:200 and the incidence of apnea, laryngospasm, stridor, or wheezing was approximately 1:400.[50] Therefore, airway interventions during PS are frequently necessary to prevent serious complications; thus, sedation personnel must be capable of immediate recognition and management of respiratory impairment. Another report from the same group included almost 50,000 PS with the administration of propofol by anesthesiologists and nonanesthesiologists providers. Like their earlier findings, major complications such as aspiration and cardiac arrest were uncommon, and no deaths were reported. The incidence of airway obstruction, apnea, laryngospasm, bronchospasm, stridor, or wheezing was 1:65,[51] suggesting that propofol is associated with a higher incidence of respiratory complications when compared with other agents. No differences in complication rates were identified when the performance of anesthesiologists were compared with nonanesthesiologists. The authors conclude that propofol can be safely used for PS when administered by well-trained and well-organized sedation groups. In their largest study to date (>130,000 patients), the Pediatric Research Consortium shows similar complication rates regardless of specialty.[52] Large studies (>25,000 infants and children) of propofol PS administered by emergency physicians and pediatric

hospitalists showed similar results with a low incidence of serious events with no long-term complications.[53,54] Data from anesthesiologists providing PS in a high-risk group (70% of patients were ASA 3 and 4) during imaging studies with propofol found 98 adverse events from almost 1500 anesthetics with no long-term complications and predictors of complications found were ASA physical status, duration of anesthetic, and presence of airway abnormalities.[55]

Across sedation studies the profile of adverse events is similar, with airway obstruction occurring most commonly followed by desaturation and apnea. Laryngospasm and hemodynamic changes were uncommon. In conclusion, well-organized sedation services that guarantee appropriate credentials and competencies in nonanesthesiologists showed low incidence of adverse events during propofol sedation suggesting a safety profile and efficacy. These results cannot be generalized to all nonanesthesiologists providers of PS.[56] Standardized definitions of the different adverse events during PS have been developed and are expected to better define the complications profile and help in to developing evidence-based care during PS and determine acceptable rates of adverse events.[57]

Allergic reactions to contrast, including anaphylaxis, are another adverse event during PS. The previous incidence of any reaction was as high as 5% with a third of these severe.[58] Improvements in the practice with the use of nonionic iodinated low-osmolality contrast have decreased the incidence to 0.18% with 80% of those mild and just 15% severe.[59] Rapid recognition, basic support, volume resuscitation, epinephrine, antihistamines, and corticosteroids constitute the mainstay therapy. Different regimens are used to premedicate with steroids and antihistamines in patients with previous allergic reactions to contrast. Usually PO steroids are given 13, 7, and 1 hour before the exposure and antihistamines 1 hour before the exposure. Severe reactions may still occur despite premedication with steroids and use of low-osmolar contrast agents. Typically, the breakthrough reaction is of similar severity to the patient's initial reaction. Children with history of severe or life-threatening reactions have a 24% risk of having a similar reaction despite the administration of corticosteroids.[60]

The radiation exposure to children is another risk. The largest exposure to radiation in the pediatric population occurs during CT studies. Children are more sensitive to radiation. Advances on CT technology have decreased the exposure to radiation. Working as a team with radiologists, referring physicians and technologists, is important to protect children of excessive and sometimes unnecessary radiation. Precontrast and postcontrast scans double or even sometimes triple the exposure to radiation.

Unique risks occur in the MRI. Magnetic field strength creates a risk environment where mishaps with ferromagnetic objects can potentially happen with disastrous consequences. New technology has increased the

power of the magnets increasing from 1.5 to 3.0 T with better image resolution, but also with stronger magnetic fields. Formal procedures, extreme vigilance, and familiarity with the MRI environment are necessary. Screening of patients and parents for the presence of a pacemaker, vascular clip, insulin pump, and cochlear implant is essential. Special precautions must be used when using infusion pumps. The use of MRI compatible infusion pumps is highly recommended. Non-MRI compatible pumps must remain distant from the MRI magnetic field or be mounted outside the MRI scanner and fitted with appropriately long extension tubing. Ferromagnetic tracheostomies in children (Bivona; Smiths Medical, Kent, UK) must be changed by nonferromagnetic tracheostomies. Besides the risk related to ferromagnetic objects, children are at risk of burns from objects that heat during MRI, malfunction of implanted devices, allergic reaction to contrast agents, and hearing impairment due to the loud noisy environment. During emergency situations, quenching of the magnet could be necessary to remove a ferromagnetic object. The magnet is made of coils of superconducting wire that requires constant cooling by helium. During quenching, there is significant risk of hypoxic mixtures due to escape of helium and risk of hearing impairment due to the extreme noisy levels. A 1.5- and a 3-T MRI reach on average 95 and 99 dB, respectively. The Occupational Safety and Health Administration mandates to limit noise exposure of 95 dB to maximum 4 hours/day and 100 dB to 2 hours/day. Therefore, patients and relatives who stay in the MRI room must wear earplugs to protect against the high-intensity sound. Neonates and infants are at risk of hypothermia in the MRI due to continuous cooling of the room, which is necessary to guarantee the function of the magnet, and the noncompatibility of air-forced warming systems in the MRI. Therefore, use of warm blankets in the neonates is imperative. Gadolinium is a low-osmolality ionic contrast agent used to enhance the MRI images. Anaphylactoid reactions are extremely uncommon, but it is associated with nephrogenic systemic fibrosis in patients with impairment in the renal function. Therefore, its administration must be avoided in patients with renal failure.[61]

Potential risks of adverse events during the recovery period mandates accessibility to basic monitoring, suction equipment, oxygen source, devices (mapleson or ambu bag) to provide positive pressure ventilation, and to specific antagonists of opioids and benzodiazepines. If the administration of an antagonist is necessary, which is extremely infrequent, continuous and prolonged monitoring is necessary given the shorter half-life of these agents with the risk of recurrent respiratory depression. The use of sedative regimens that includes the administration of reversal agents is not recommended.[28] An intravenous access must be maintained until the anesthesia provider considers the risk of having adverse events is minimum.[28] Specific discharge criteria include recovery of the level of consciousness and stable vital signs. Parents must

be contacted within 24 hours of the procedure to evaluate the quality of care and detect late complications.

A PS database that includes complications provides input about the incidence and profile of the adverse events not only the most severe (respiratory and cardiovascular depression) but also untoward events such as failed sedation, paradoxical reactions, prolonged sedation, nausea, and vomiting.

Future of Pediatric Sedation

Pediatric sedation has undergone tremendous change during the past decade driven by a cultural shift that demands aggressive management of pain and anxiety in hospitalized children. New and safer sedative agents, using other alternative options for PS, changing the nature of education by using simulation, and finally collecting data from multispecialties to better determine and prevent adverse events are expecting changes in the practice of PS.

Improving Sedation Provider Training Education and Curriculum

The heterogenous guidelines followed by the diverse group of practitioners providing PS, and the varied environments in which care occurs, challenge us to provide uniformly safe and effective PS. It is imperative that practitioners performing pediatric PS have the requisite knowledge and medical skills demanded by this dynamic clinical environment. Unfortunately, many nonanesthesiologists are inadequately trained to respond to these challenges, putting children at risk. This training gap was highlighted in a recent study in which pediatric residents were unable to intubate the trachea of a child on the first attempt in almost 50% of cases.[62] Therefore, competency-related factors are important to improve practitioner training and ongoing maintenance of skills, as well as having rigorous credentialing procedures in place that ensure PS competency.

Individuals providing sedation must be capable of performing a presedation evaluation, have a depth knowledge of the sedation pharmacologic armamentarium, be skilled in the recognition and treatment of cardiopulmonary events, and have a thorough understanding of sedation procedures including monitoring, consent, recovery, and fasting guidelines. It is imperative that providers determine when the planned procedure, or the gravity of underlying disease in the child, precludes the use of sedation by a nonanesthesiologist. Practitioners must also recognize when and how to engage their emergency back-up systems in their unique practice environment. Basic credentials should include certification in Pediatric Advanced Life Support, Advanced Trauma Life Support, Adavanced Cardiovascular Life Support, or Neonatal Resuscitation

Program. Furthermore, ongoing sedation education should be incorporated into each practitioner's maintenance of privileges.

Simulation in Pediatric Sedation

One of the most exciting training innovations in medicine has been the development of high-fidelity simulation. Similar to other high-risk organizations such as the aviation and nuclear power industries, medical simulation is emerging as a powerful and broadly applicable educational tool capable of exploring technical, behavioral, and systems issues within health care. Simulation is a technique that replaces or amplifies real experiences with guided experiences that evoke or replicate substantial aspects of the real world in a fully interactive manner.[63,64] It allows the representation of a clinical event for the purpose of learning, practicing, evaluating, testing, and understanding human actions.[63] Simulation allows a specific lesson to be learned through experience that can be adjusted and repeated to suit the needs of the practitioner and institution, without putting patients at risk and also incorporating a review of educational content and debriefing by an expert facilitator to drive learning.[63]

Emerging studies explore how simulation enhances pediatric sedation practice. A study in pediatricians compares a group that trained with simulation with those who did not and demonstrated that safety was enhanced when simulation was incorporated into physician training.[10] Simulation also addresses systemic failures that undermine patient safety. These systems-based "waiting to happen" issues are referred to as "latent errors." Blike et al[65] utilized simulation to evaluate latent errors impacting patient safety in children undergoing PS demonstrating that children in some clinical areas were at greater risk for prolonged hypoxemia than other areas. The authors argue that simulation provides a unique tool capable of exploring patient vulnerabilities in complex health care environments.

Studies evaluating performance among pediatric trainees demonstrate clear deficiencies in life-saving skills such as resuscitation and airway management.[66,67] Medical simulation has tremendous potential to fill this gap between knowledge and action in an environment that is controllable, reproducible, and safe. Although there is a lack of strong evidence that simulation improves patient safety and outcomes, we are confident that pediatric simulation will emerge as a powerful tool for practitioner development and assessment, as well as a means to examine the functionality of health care systems.

■ Conclusions

Pediatric anesthesiologists play a critical role on defining the competencies necessary among the different practitioners to provide pediatric PS. Consensus among the different specialties is critical.

Without this kind of cooperation and coordination between all providers, we will not be able to identify hazards and vulnerabilities and eventually will not be able to create and maintain a safe, productive, and efficient environment for pediatric sedation.

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■ References

1. Mason KP. Sedation trends in the 21st century: the transition to dexmedetomidine for radiological imaging studies. *Paediatr Anaesth*. 2010;20:265–272.
2. Krauss B, Green SM. Procedural sedation and analgesia in children. *Lancet*. 2006;367:766–780.
3. Cravero JP, Blike GT. Review of pediatric sedation. *Anesth Analg*. 2004;99:1355–1364.
4. Krauss B, Green SM. Training and credentialing in procedural sedation and analgesia in children: lessons from the United States model. *Paediatr Anaesth*. 2008;18:30–35.
5. Cote CJ, Wilson S. Guidelines for monitoring and management of pediatric patients during and after sedation for diagnostic and therapeutic procedures: an update. *Pediatrics*. 2006;118:2587–2602.
6. Goodson JM, Moore PA. Life-threatening reactions after pedodontic sedation: an assessment of narcotic, local anesthetic, and antiemetic drug interaction. *J Am Dent Assoc*. 1983;107:239–245.
7. CMS Guidelines Centers for Medicare and Medicaid Services. CMS Manual System. Pub 100-07 State Operations Provider Certification. Appendix A. 42 CFR. Section 482.52. Revised hospital anesthesia services interpretive guidelines. Available at: http://www.cms.gov/SurveyCertificationgeninfo/downloads/SCLetter11_10.pdf. Accessed December 2, 2011.
8. Statement on Granting Privileges for Administration of Moderate Sedation to Practitioners Who Are Not Anesthesia Professionals. Available at: http://www.asahq.org/For-Members/Standards-Guidelines-and-Statements.aspx. Accessed October 19, 2011.
9. American Society of Anesthesiologists. Statement on Granting Privileges to Non-anesthesiologist Physicians for Personally Administering or Supervising Deep Sedation. Available at: http://www.asahq.org/For-Members/Standards-Guidelines-and-Statements.aspx. Accessed October 20, 2010.
10. Shavit I, Keidan I, Hoffmann Y, et al. Enhancing patient safety during pediatric sedation: the impact of simulation-based training of nonanesthesiologists. *Arch Pediatr Adolesc Med*. 2007;161:740–743.
11. Leroy PL, Schipper DM, Knape HJ. Professional skills and competence for safe and effective procedural sedation in children: recommendations based on a systematic review of the literature. *Int J Pediatr*. 2010;2010:934298.
12. Malviya S, Voepel-Lewis T, Tait AR. Adverse events and risk factors associated with the sedation of children by nonanesthesiologists. *Anesth Analg*. 1997;85:1207–1213.
13. Ramsay MA, Savege TM, Simpson BR, et al. Controlled sedation with alphaxalone-alphadolone. *Br Med J*. 1974;2:656–659.
14. Chernik DA, Gillings D, Laine H, et al. Validity and reliability of the Observer's Assessment of Alertness/Sedation Scale: study with intravenous midazolam. *J Clin Psychopharmacol*. 1990;10:244–251.
15. Ambuel B, Hamlett KW, Marx CM, et al. Assessing distress in pediatric intensive care environments: the COMFORT scale. *J Pediatr Psychol*. 1992;17:95–109.

16. Malviya S, Voepel-Lewis T, Eldevik OP, et al. Sedation and general anaesthesia in children undergoing MRI and CT: adverse events and outcomes. *Br J Anaesth*. 2000;84:743–748.
17. Cravero JP, Blike GT, Surgenor SD, et al. Development and validation of the Dartmouth Operative Conditions Scale. *Anesth Analg*. 2005;100:1614–1621.
18. Green SM, Mason KP. Reformulation of the sedation continuum. *JAMA*. 2010;303:876–877.
19. Green SM, Mason KP. Stratification of sedation risk—a challenge to the sedation continuum. *Paediatr Anaesth*. 2011;21:924–931.
20. American Society of Anesthesiologists C. Practice guidelines for preoperative fasting and the use of pharmacologic agents to reduce the risk of pulmonary aspiration: application to healthy patients undergoing elective procedures: an updated report by the American Society of Anesthesiologists Committee on Standards and Practice Parameters. *Anesthesiology*. 2011;114:495–511.
21. Green SM, Roback MG, Miner JR, et al. Fasting and emergency department procedural sedation and analgesia: a consensus-based clinical practice advisory. *Ann Emerg Med*. 2007;49:454–461.
22. Agrawal D, Manzi SF, Gupta R, et al. Preprocedural fasting state and adverse events in children undergoing procedural sedation and analgesia in a pediatric emergency department. *Ann Emerg Med*. 2003;42:636–646.
23. Sanborn PA, Michna E, Zurakowski D, et al. Adverse cardiovascular and respiratory events during sedation of pediatric patients for imaging examinations. *Radiology*. 2005;237:288–294.
24. Warner MA, Warner ME, Weber JG. Clinical significance of pulmonary aspiration during the perioperative period. *Anesthesiology*. 1993;78:56–62.
25. Krauss B, Green SM. Sedation and analgesia for procedures in children. *N Engl J Med*. 2000;342:938–945.
26. Mahmoud M, McAuliffe J, Kim HY, et al. Oral contrast for abdominal computed tomography in children: the effects on gastric fluid volume. *Anesth Analg*. 2010;111:1252–1258.
27. Mahmoud M, McAuliffe J, Donnelly LF. Administration of enteric contrast material before abdominal CT in children: current practices and controversies. *Pediatr Radiol*. 2011;41:409–412.
28. Gross J, Bailey PL, Connis RT, et al. Practice guidelines for sedation and analgesia by non-anesthesiologists. *Anesthesiology*. 2002;96:1004–1017.
29. Hackel A, Badgwell JM, Binding RR, et al. Guidelines for the pediatric perioperative anesthesia environment. American Academy of Pediatrics. Section on Anesthesiology. *Pediatrics*. 1999;103:512–515.
30. Brown TR, Goldstein B, Little J. Severe burns resulting from magnetic resonance imaging with cardiopulmonary monitoring. Risks and relevant safety precautions. *American J Phys Med Rehabil*. 1993;72:166–167.
31. Mason KP, Zurakowski D, Connor L, et al. Infant sedation for MR imaging and CT: oral versus intravenous pentobarbital. *Radiology*. 2004;233:723–728.
32. Rooks VJ, Chung T, Connor L, et al. Comparison of oral pentobarbital sodium (nembutal) and oral chloral hydrate for sedation of infants during radiologic imaging: preliminary results. *Am J Roentgenol*. 2003;180:1125–1128.
33. Spear RM, Waldman JY, Canada HM, et al. Intravenous thiopentone for CT and MRI in children. *Pediatric Anesthesia*. 1993;3:29–32.
34. Rockoff MA, Goudsouzian NG. Seizures induced by methohexital. *Anesthesiology*. 1981;54:333–335.
35. Nelson LE, Lu J, Guo T, et al. The alpha2-adrenoceptor agonist dexmedetomidine converges on an endogenous sleep-promoting pathway to exert its sedative effects. *Anesthesiology*. 2003;98:428–436.

36. Mason KP, O'Mahony E, Zurakowski D, et al. Effects of dexmedetomidine sedation on the EEG in children. *Paediatr Anaesth*. 2009;19:1175–1183.
37. Mahmoud M, Radhakrishman R, Gunter J, et al. Effect of increasing depth of dexmedetomidine anesthesia on upper airway morphology in children. *Paediatr Anaesth*. 2010;20:506–515.
38. Mahmoud M, Gunter J, Donnelly LF, et al. A comparison of dexmedetomidine with propofol for magnetic resonance imaging sleep studies in children. *Anesth Analg*. 2009;109:745–753.
39. Mason KP, Zurakowski D, Zgleszewski S, et al. Incidence and predictors of hypertension during high-dose dexmedetomidine sedation for pediatric MRI. *Paediatr Anaesth*. 2010;20:516–523.
40. Mason KP, Zgleszewski S, Forman RE, et al. An exaggerated hypertensive response to glycopyrrolate therapy for bradycardia associated with high-dose dexmedetomidine. *Anesth Analg*. 2009;108:906–908.
41. Hostetler MA, Davis CO. Prospective age-based comparison of behavioral reactions occurring after ketamine sedation in the ED. *Am J Emerg Med*. 2002;20:463–468.
42. Green SM, Roback MG, Krauss B, et al. Predictors of airway and respiratory adverse events with ketamine sedation in the emergency department: an individual-patient data meta-analysis of 8,282 children. *Ann Emerg Med*. 2009;54:158–168; e151-e154.
43. Mason KP, Sanborn P, Zurakowski D, et al. Superiority of pentobarbital versus chloral hydrate for sedation in infants during imaging. *Radiology*. 2004;230:537–542.
44. Zier JL, Doescher JS. Seizures temporally associated with nitrous oxide administration for pediatric procedural sedation. *J Child Neurol*. 2010;25:1517–1520.
45. Akin A, Esmaoglu A, Guler G, et al. Propofol and propofol-ketamine in pediatric patients undergoing cardiac catheterization. *Pediatr Cardiol*. 2005;26:553–557.
46. Kogan A, Efrat R, Katz J, et al. Propofol-ketamine mixture for anesthesia in pediatric patients undergoing cardiac catheterization. *J Cardiothorac Vasc Anesth*. 2003;17:691–693.
47. Tosun Z, Esmaoglu A, Coruh A. Propofol-ketamine vs propofol-fentanyl combinations for deep sedation and analgesia in pediatric patients undergoing burn dressing changes. *Paediatr Anaesth*. 2008;18:43–47.
48. Arora S. Combining ketamine and propofol ("ketofol") for emergency department procedural sedation and analgesia: a review. *West J Emerg Med*. 2008;9:20–23.
49. Badrinath S, Avramov MN, Shadrick M, et al. The use of a ketamine-propofol combination during monitored anesthesia care. *Anesth Analg*. 2000;90:858–862.
50. Cravero JP, Blike GT, Beach M, et al. Incidence and nature of adverse events during pediatric sedation/anesthesia for procedures outside the operating room: report from the Pediatric Sedation Research Consortium. *Pediatrics*. 2006;118:1087–1096.
51. Cravero JP, Beach ML, Blike GT, et al. The incidence and nature of adverse events during pediatric sedation/anesthesia with propofol for procedures outside the operating room: a report from the Pediatric Sedation Research Consortium. *Anesth Analg*. 2009;108:795–804.
52. Couloures KG, Beach M, Cravero JP, et al. pact of provider specialty on pediatric procedural sedation complication rates. *Pediatrics*. 2011;127:e1154–e1160.
53. Srinivasan M, Turmelle M, Depalma LM, et al. Procedural sedation for diagnostic imaging in children by pediatric hospitalists using propofol: analysis of the nature, frequency, and predictors of adverse events and interventions. *J Pediatr*. 2012;160:801–806; e801.
54. Mallory MD, Baxter AL, Yanosky DJ, et al. Emergency physician-administered propofol sedation: a report on 25,433 sedations from the pediatric sedation research consortium. *Ann Emerg Med*. 2011;57:462–468; e461.
55. Kiringoda R, Thurm AE, Hirschtritt ME, et al. Risks of propofol sedation/anesthesia for imaging studies in pediatric research: eight years of experience in a clinical research center. *Arch Pediatr Adolesc Med*. 2010;164:554–560.

56. Havidich JE, Cravero JP. The current status of procedural sedation for pediatric patients in out-of-operating room locations. *Curr Opin Anaesthesiol*. 2012;25:453–460.
57. Bhatt M, Kennedy RM, Osmond MH, et al. Consensus-based recommendations for standardizing terminology and reporting adverse events for emergency department procedural sedation and analgesia in children. *Ann Emerg Med*. 2009;53:426–435; e424.
58. Goldberg M. Systemic reactions to intravascular contrast media. A guide for the anesthesiologist. *Anesthesiology*. 1984;60:46–56.
59. Dillman JR, Strouse PJ, Ellis JH, et al. Incidence and severity of acute allergic-like reactions to i.v. nonionic iodinated contrast material in children. *Am J Roentgenol*. 2007;188:1643–1647.
60. Freed KS, Leder RA, Alexander C, et al. Breakthrough adverse reactions to low-osmolar contrast media after steroid premedication. *Am J Roentgenol*. 2001;176:1389–1392.
61. Ehrenwerth J, Singleton MA, Bell C, et al. Practice advisory on anesthetic care for magnetic resonance imaging: a report by the Society of Anesthesiologists Task Force on Anesthetic Care for Magnetic Resonance Imaging. *Anesthesiology*. 2009;110: 459–479.
62. Kerrey BT, Rinderknecht AS, Geis GL, et al. Rapid sequence intubation for pediatric emergency patients: higher frequency of failed attempts and adverse effects found by video review. *Ann Emerg Med*. 2012;60:251–259.
63. Gaba DM. The future vision of simulation in health care. *Qual Saf Health Care*. 2004;13(suppl 1):i2–i10.
64. Voelker R. Medical simulation gets real. *JAMA*. 2009;302:2190–2192.
65. Blike GT, Christoffersen K, Cravero JP, et al. A method for measuring system safety and latent errors associated with pediatric procedural sedation. *Anesth Analg*. 2005;101:48–58; Table of contents.
66. Nadel FM, Lavelle JM, Fein JA, et al. Assessing pediatric senior residents' training in resuscitation: fund of knowledge, technical skills, and perception of confidence. *Pediatr Emerg Care*. 2000;16:73–76.
67. O'Donnell CP, Kamlin CO, Davis PG, et al. Endotracheal intubation attempts during neonatal resuscitation: success rates, duration, and adverse effects. *Pediatrics*. 2006;117:e16–e21.