The Anesthesia Directed Sedation Service: Models, Protocols, and Challenges

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Children undergo painful or distressing procedures in remote locations where anesthesia providers (anesthesiologists, certified registered nurse anesthetists, anesthesia assistants) are not always readily available. In these situations, sedation models with nonanesthesia care providers are necessary to fill the void that anesthesia services cannot provide. Many procedures do not require general anesthesia (even for the pediatric population), and may be accomplished with varying depths of sedation. Anesthesia, as a specialty, offers a special expertise which can be applied to the development, oversight, and implementation of a sedation service. Anesthesiologists already have knowledge of sedatives, analgesics, and anesthetics and possess the advanced intervention skills necessary to rescue from respiratory and hemodynamic compromise. This specialty has taken an active role in establishing guidelines and standards for the sedation of both adults and children over several decades. In addition, the Institute of Medicine recognizes the field of anesthesia as a model of patient safety: anesthesia associated mortality is currently considered to be as low as 1/200,000 or 300,000 anesthetics administered [1]. Sedation can be considered to be an extension of the specialty: knowledge of the cardiovascular and respiratory physiology, as well as the pharmacology of sedative agents are inherent to this discipline.

Anesthesiologists have contributed a great deal to the development and improvement of the practice of sedation. Historically, one of their most significant contributions was the development of pediatric sedation guidelines in 1983 (published in 1985) [2]. The impetus behind the establishment of these guidelines was a sentinel event, in response to three deaths in a single dental office [3]. These guidelines primarily developed the framework for guidelines which were eventually proposed by the Joint Commission [4].

Some of these initial concepts and recommendations continue to be followed in current practice: The need for informed consent, appropriate fasting before sedation, monitoring of vital signs, and the need for basic life support (BLS) skills. It was also at this stage that the concept of an independent observer for deeply sedated patients was introduced [2]. The only responsibility of this observer was to monitor the patient. The independent observer status would eventually evolve to encompass the administration of medications as well.

Almost 20 years later, the pediatric guidelines were amended in 2002, at which time the term "conscious sedation" [5] was retired. The term "conscious sedation" was viewed a misnomer, an inaccurate representation of the sedated state. In response to the growing demand for sedation standards for non-anesthesiologists, the American Society of Anesthesiology (ASA) first created

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sedation guidelines for nonanesthesiologists in 1996 [6]. Additional guidelines for credentialing nonanesthesiologists were published in 2002 [7] and amended in 2004 [8, 9]. These guidelines introduced capnography as an available, but not required, monitor for moderate sedation. The American Society of Anesthesiologists updated in July, 2011 the Standards for Basic Anesthetic Monitoring [10]. These standards specify that "during moderate or deep sedation the adequacy of ventilation shall be evaluated by continual observation of qualitative clinical signs and monitoring for the presence of exhaled carbon dioxide unless precluded or invalidated by the nature of the patient, procedure or equipment." Many organizations, including the American Academy of Pediatrics (AAP) and the American Academy of Pediatric Dentistry (AAPD) have incorporated these guidelines into their own practice [11].

While anesthesiologists have created and set the standards for sedation, their availability and ability to meet the growing demand for sedation by being direct caregivers, remains untenable. As the demand for sedation services increase, so does the demand for anesthesia resources in ambulatory centers and satellite areas within and separate from the hospital. In response to the limited number of anesthesia providers, a multispeciality service model has evolved in the United States over the past decade [12]. As a result, many different medical specialties, such as Emergency Medicine, Gastroenterology, Intensive Care Medicine, Hospital Medicine, Pediatrics, and Radiology, established sedation services within their own specialties. In the United States, all these medical subspecialties follow sedation guidelines set by the Joint Commission but morph them to fulfill their unique needs within their own environment. In fact, such organizations, over the years, have gained substantial experience in sedation and considered themselves to be experts in this field. As a result, it is no surprise that anesthesia's involvement in sedation services has been slowly diminishing. In 2005, a survey that was conducted in North America showed that only half of the respondents had indicated that they had a formal sedation service [13]. What was even more surprising was that when only one type of institution-wide service was provided, only 26% of such services involved either pediatric or general anesthesiologists [13].

The apparent diminishing presence of anesthesiologists is initially concerning and seems intuitively counterproductive. In fact, the shortage of providers, particularly anesthesiologists, has been considered to be the most common barrier to the development of a pediatric sedation service [13]. In response to this shortage, many institutions requested that anesthesia departments develop institutional guidelines for provision of sedation by nonanesthesiologists [14]. Initially, anesthesia departments appeared apathetic and disinterested, more focused on meeting the rising demand for anesthesiologists in satellite operating rooms, separate from the operating room. The economics of anesthesia practice relied heavily on revenue generated from the operating room and that area took priority. An editorial written by Wetzel, in Anesthesia and Analgesia in 2006, asked whether it was justifiable to refuse or provide care and, in turn, forbid others from providing such care [15]. He eloquently stated that:

> We cannot eschew responsibility when the solution remains ours.

Development of Protocols

Pediatric anesthesiologists have at their disposal a wide armamentarium of drugs for sedation; many of these medications, such as remifentanil, have a lower margin of safety, but confer some advantages. Table 12.1 is a summary of sedation regimens that have been used by anesthesiologists [16]. Nonanesthesiologists, for the most part, have relied on a more limited array of older and more established medications such as chloral hydrate, pentobarbital, ketamine, and midazolam for many of their procedures [17–23]. There is, however, a willingness and enthusiasm among many of them to expand their expertise in using other sedation medications. While this may mean a better sedation experience for patients, the matter is not without controversy. For example, the use of propofol by nonanesthesiologists engenders such controversy that it has created rifts between specialties [24–27].

Table 12.1 Sedation regimens for children

Drug regimen	Dose/route of administration	Comments (general citations at end of text)
Propofol	100–100 μg/kg/min IV	Ideal agent for nonpainful diagnostic procedures. Only for use by expert airway managers with good back-up systems [62–64]
Pentobarbitol	4–6 mg/kg IV or PO	Long history of effective use in radiology imaging. Emergence can be prolonged [65, 66]
Midazolam	0.5–0.75 mg/kg PO 0.025–0.5 mg/kg IV 0.2 mg/kg intranasal	Track record of safe use both PO and IV. Paradoxical reactions are not infrequent. Intranasal route is so irritating we do not recommend it [67–69]
Chloral hydrate	50–100 mg/kg PO	Still the most popular drug for radiologic sedation in community hospitals. Prolonged sedation and paradoxical reactions are reported. Monitoring required [62, 66, 70]
Etomidate	0.1–0.4 mg/kg IV	Emerging use in emergency medicine for brief painful procedures, although no intrinsic analgesic effect [71–73]
		Post-sedation nausea reported. Little effect on heart rate and blood pressure in most cases.
Methohexital (not readily available at this time)	0.25–0.50 mg/kg IV 20–25 mg/kg rectal	Effective sedation in IV form. Rectal route is not recommended because of high frequency of apnea/desaturation events [74–76]
Propofol with fentanyl	Fentanyl 1–2 μg/kg IV with propofol 50–150 μg/kg IV	Best for deep sedation/anesthesia. Risk of requiring advanced airway management is high [77, 78]
Midazolam with fentanyl	Midozolam 0.020 mg/kg IV Fentanyl 1–2 μg/kg IV	Most common combination for painful procedures in the emergency department. Risk of apnea and hypoxia is significant [79, 80]
Ketamine	3–4 mg/kg IM	Effective sedation and analgesia for painful procedures
	1–2 mg/kg IV	Relatively, common nausea and vomiting after procedure. Laryngospasm reported [81–83]
		Best if combined with an anticholinergic for control of secretions. Combination with midazolam is common, although effectiveness in treating emergence dysphoria is debated
Remifentanil	0.1 μg/kg/min	Emerging use in pediatric sedation, exclusively by anesthesiologists at this point – apnea a significant risk [77, 84–86]
Nitrous oxide	50% in 50% oxygen, up to 70% used by some	Long history of safe use providing moderate sedation for minimally and moderately painful procedures. Care must be taken when used in addition to other sedatives (local anesthetics) where deep sedation can easily result [87–89]

Note: This table shows different medications that are currently used in procedural sedation, with an explanation regarding its use in common practice
Source: From Cravero and Blike [16]. Reprinted with permission from Wolters Kluwer Health

Controversies aside, as the proliferation of different drug regimens continue, particularly among nonanesthesiologists, it may be more prudent to redirect efforts to strengthening the credentialing and training process, rather than restrict certain sedative use. Realistically, it is likely that the term "deep sedation" in children could very well mean periods of general anesthesia. "Conscious sedation" in children is anything but conscious [28]. It seems intuitive then that the skills required to "rescue" a patient from a deep sedation which has progressed to general anesthesia needs careful delineation.

An Anesthesia-Supervised Sedation Team

> Anesthesiologists possess specific expertise in the pharmacology, physiology, and clinical management of patients receiving sedation and analgesia [7].

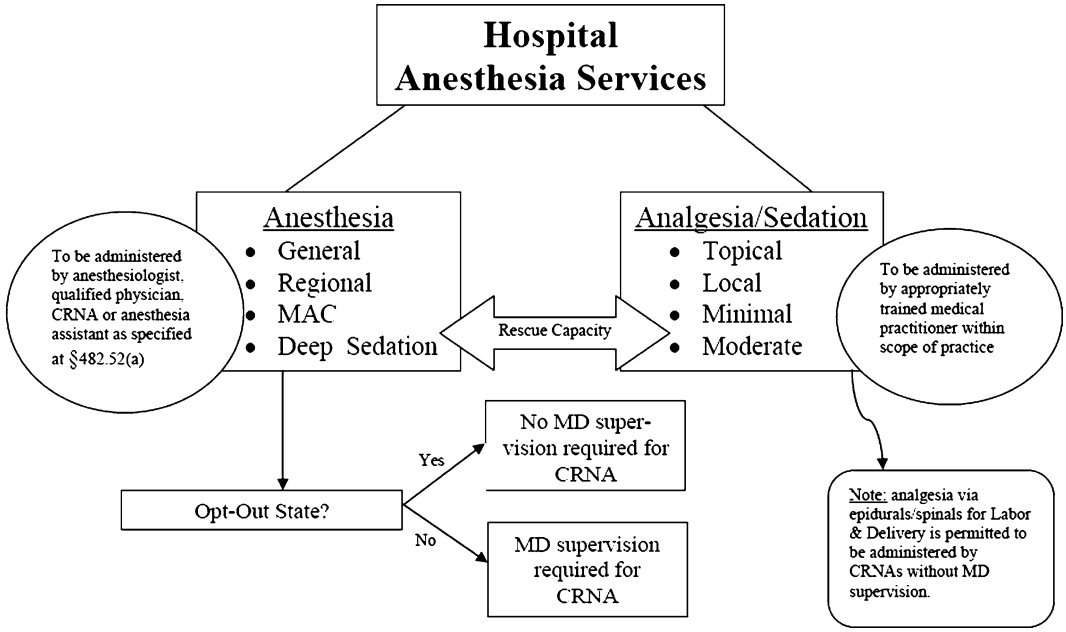

Fig. 12.1 Center for Medicare and Medicaid Services (CMS) revised Hospital Anesthesia Services Interpretive Guidelines – State Operations Manual (SOM) Appendix A [32]. The guidelines presented a proposed organization plan for Hospital Anesthesia Services [32]

Anesthesiologists are trained and proficient in the administration of sedation and have the necessary advanced skills to rescue from any depth of sedation or an inadvertent anesthetic. Providing an anesthesia-delivered sedation service has many challenges. Sedation services are often provided outside the operating room, almost always in areas that are less familiar to the anesthesiologist. The operating room, on the other hand, is definitely within the comfort zone of anesthesia personnel where there is an inherent level of consistency with regard to equipment, space, medications, and availability of help nearby. The delivery of anesthesia in the operating room needs skills in problem recognition and management. These skills may be developed through training that applies a cockpit or pilot response management model designed to promote vigilance and situational awareness [29–31]. Although the pattern of anesthesia delivery in the operating room cannot be precisely duplicated in areas outside the operating room, these training programs can be applied to simulated sedation scenarios outside of the operating room.

Anesthesia-led sedation services consist of different models. In one model, there are anesthesia directed and administered sedation services. All sedation is administered by anesthesiologists or nurse anesthetists. This model has some advantages: anesthesia providers may deliver sedation, monitored anesthesia care (MAC), or general anesthesia, thereby capable of providing all services. The ability to provide all levels of sedation, deep sedation included, is an advantage to an anesthetic care provider model. In February 2010, the Center for Medicare and Medicaid Services (CMS) revised the Hospital Anesthesia Services Interpretive Guidelines – State Operations Manual (SOM) Appendix A [32]. The guidelines presented a proposed organization plan for Hospital Anesthesia Services [32] (see Fig. 12.1). Important amendments included the recognition of deep sedation as a service which falls under MAC. Moderate sedation, in contrast, did not fall under the requirement for anesthesia administration and supervision. MAC according to these guidelines could only be administered by:

1. A qualified anesthesiologist
2. An MD or DO (other than an anesthesiologist)

3. A dentist, oral surgeon, or podiatrist who is qualified to administer anesthesia under State law
4. A CRNA who is supervised by the operating practitioner or by an anesthesiologist who is immediately available if needed

   A CRNA is defined in §410.69(b) as a "…registered nurse who: (1) is licensed as a registered professional nurse by the State in which the nurse practices; (2) meets any licensure requirements the State imposes with respect to non-physician anesthetists; (3) has graduated from a nurse anesthesia educational program that meets the standards of the Council on Accreditation of Nurse Anesthesia Programs, or such other accreditation organization as may be designated by the Secretary; and (4) meets the following criteria: (i) has passed a certification examination of the Council on Certification of Nurse Anesthetists, the Council on Recertification of Nurse Anesthetists, or any other certification organization that may be designated by the Secretary; or (ii) is a graduate of a program described in paragraph (3) of this definition and within 24 months after that graduation meets the requirements of paragraph (4)(i) of this definition" [32].

5. An anesthesiologist's assistant under the supervision of an anesthesiologist who is immediately available if needed

   An anesthesiologist's assistant is defined in §410.69(b) as a "…person who – (1) works under the direction of an anesthesiologist; (2) is in compliance with all applicable requirements of State law, including any licensure requirements the State imposes on nonphysician anesthetists; and (3) is a graduate of a medical school-based anesthesiologist's assistant education program that – (A) is accredited by the Committee on Allied Health Education and Accreditation; and (B) includes approximately two years of specialized basic science and clinical education in anesthesia at a level that builds on a premedical undergraduate science background" [32].

Subsequent to these guidelines, sedation programs which had relied on non-CMS-approved providers to deliver deep sedation, now elected to alter their delivery model. Children's Hospital Boston is one such example. Prior to 2010, the Department of Anesthesia had organized, directed, written protocols for, and directly supervised sedation administered by Registered Nurses [22, 33–37]. The concept of a nurse-led sedation team is not new, and it has been described in hospitals even as early as two decades ago [38, 39]. These nurses were trained in Pediatric Advanced Life Support (PALS) as well as Basic Life Support (BLS). They completed on-line web-based teaching tools that were specific to sedation agents and regimen. Most nurses had critical care or emergency medicine background and had worked in pediatrics. Subsequent to the revised CMS guidelines [32], Children's Hospital Boston altered their sedation model by replacing these registered nurses with nurse anesthetists, a physician, anesthesiologists, anesthesia residents, and anesthesia fellows. All deep sedation now conforms to the February 2010 CMS guidelines.

Nursing administered sedation programs are still prevalent in the United States. Careful physician oversight provides clear boundaries for sedation practice. One such example is the University of Iowa: The University of Iowa continues to maintain a Nurse Sedation Program. In most cases, the level of sedation provided by their sedation nurses is mild to moderate, with a unique model which incorporates propofol administration by registered nurses [40].

Protocols

Protocols developed by anesthesiologists are primarily created for use by nonanesthesiologists. The expertise and knowledge base of anesthesiologists has helped to design-training programs that not only teach sedation related skills, but also evaluate competencies of nonanesthesiologists in all aspects of sedation. The training and teaching can include airway skills, pharmacology of sedation drugs, development of specific drug protocols and collection of Quality Assurance data. In addition to creating such a program, they also have the expertise to monitor sedation practices within an institution. Anesthesiologists have particular expertise and experience in using more than one drug for a sedation event. Their experience in titrating two or more drugs which have potential respiratory and hemodynamic effects has been very useful in developing protocols. We shall describe a few of the drug protocols developed primarily by anesthesiologists.

Ketamine

Ketamine has been used as an adjunct analgesic and hypnotic medication for many procedures. The analgesic effects of ketamine are present in plasma concentrations that are significantly lower than those producing hypnosis (0.2 vs. 1.5–2.5 μg/mL) [41].

A sedation protocol using intravenous (IV) ketamine for radiological procedures is being successfully used by radiology nurses at Children's Hospital Boston. During the development of the protocol, ketamine doses and administration methods were studied and refined according to patient outcomes [21]. The outcomes of sedated patients relies on an adequate screening process whereby patients were selected based on established criteria for nurse sedation, without any contraindications to ketamine use (see Fig. 12.2) [21]. There were many procedures that took less than 10 min duration. An intramuscular ketamine protocol was developed for children without IV access who required sedation for insertion of a peripherally inserted central catheter (PICC) (see Fig. 12.3) [21]. The IV ketamine protocol was also developed to require the use of an infusion of ketamine for procedures longer than 10 min (see Fig. 12.4) [21]. The ability of radiologists to use this protocol independently for a select group of patients has allowed increased flexibility in scheduling of these cases, as well as provided an alternative to general anesthesia. However, the authors do recommend that an anesthesiologist be immediately available for airway emergencies [21].

CONTRAINDICATIONS TO USE OF KETAMINE

1. Active pulmonary infection or disease
2. Know or potential (ie, risk of) airway compromise
3. Pulmonary hypertension
4. Age of 3 months or younger
5. History of apnea, obstructive sleep apnea
6. Craniofacial defect that would make mast ventilation difficult
7. Complex caridiac disease
8. Intracranial hypertension (ie, central nervous system mass lesions, hydrocephalus, head injuries associated with increased intracranial pressure); IF THERE IS ANY DOUBT, PLEASE HAVE RADIOLOGIST CONSULT ORDERING PHYSICIAN TO DETERMINE WHETHER THERE IS INCREASED INTRACRANIAL PRESSURE RISK
9. Acute globe injury
10. Prior adverse reactions to ketamine
11. History of bipolar disease or schizophrenia
12. Head injury associated with loss of consciousness, altered mental status, or emesis
13. Any child in whom there is a question of increased intracranial pressure
14. Child with a potential ventriculoperitoneal shunt malfunction
15. Patient or parent refusal
16. Increased intraocular pressure

Fig. 12.2 This figure outlines the contraindications on the use of ketamine in the protocol used by Children's Hospital Boston for procedural sedation [21]

Ketamine has also been used as an adjunct with propofol to provide adequate conditions for performing procedures. Though ketamine has analgesic effects, it is believed that using it as an adjunct would allow lower doses of propofol to achieve the appropriate sedation level. A protocol created for auditory testing (ABR), created by Akin et al., showed that addition of ketamine of 0.5 mg/kg to an initial dose of 1.5 mg/kg of propofol in kids aged 1–13 years decreased the need for additional boluses of propofol at half the starting dose [42]. Quite often, ketamine is used in combination with propofol for procedures associated with pain. A study performed by Tosun et al., showed that the combination of propofol and ketamine was very effective for pediatric burn dressing changes [43]. In fact, it was found to be superior to using a propofol-fentanyl combination since more restlessness was found in the propofol-fentanyl group. In this study, the propofol-ketamine group received 1 mg/kg ketamine and 1.2 mg/kg propofol, and the propofol-fentanyl group received 1 μg/kg of fentanyl and 1.2 mg/kg of propofol for sedation induction. Additional propofol (0.5–1 mg/kg) was administered, as necessary, for discomfort. A very similar study using the same drug combinations and doses, in which a ketamine-propofol combination was compared to ketamine and fentanyl [44], was performed for upper endoscopic procedures. The propofol-ketamine combination provided better tolerance of the endoscope insertion and better hemodynamic stability. However, there were more side effects with ketamine such as dizziness, diplopia, and vomiting. Restlessness during endoscopy was observed more often in the propofol-fentanyl group than in the propofol-ketamine group.

INTRAMUSCULAR KETAMINE FOR PROCEDURES (ONLY FOR PICC LINE PROCEDURE OR AFTER ≥ 3 FAILED IV ATTEMPTS(FILL IN BELOW)

☐ **<5 YEARS OF AGE**

Glycopyrrolate 0.005 mg/kg x_____kg = _____ mg IM x1

Ketamine 4 mg/kg x _____kg= _____ mg (max 200 mg/dose)Mx1

Mix together in one syringe and give IM x 1 in deltoid. Use concentrated form of ketamine (100 mg/mL).

May repeat Ketamine 2 mg/kg x _____kg = _____mg (max 100 mg/dose) IM x 1 after 45 minutes.

☐ **≥5 YEARS OF AGE**

Glycopyrrolate 0.005 mg/kg x_____kg = _____ mg IM x1

Midazolam 0.1 mg/kg x _____kg = _____ mg (max 3 mg/dose) IM x 1

Ketamine 1 mg/kg x _____kg = _____ mg (max 200 mg/dose) IM x 1

Mix together in one syringe and give IM x 1 in deltoid. Use concentrated form of ketamine (100 mg/mL).

May repeat Ketamine 2 mg/kg x _____ kg = _____ mg (max 100 mg/dose) IM x 1 after 45 minutes.

Fig. 12.3 This protocol is primarily for ketamine use when intravenous access is difficult or not attainable. The age groups are divided into children less than 5 years and children greater than 5 years [21]

INTRAVENOUS KETAMINE FOR PROCEDURES <10 MINUTES (FILL IN BELOW)

☐ **<5 YEARS OF AGE**

Glycopyrrolate 0.005 mg/kg x _____ kg = _____mg IV x1

Ketamine 1 mg/kg x _____kg = _____ mg (max 70 mg/dose) IV x1.
May repeat x 1 dose if patient still responsive to nailbed pressure after 1 minute.

☐ **≥5 YEARS OF AGE**

Glycopyrrolate 0.005 mg/kg x _____ kg = _____mg IV x1

Midazolam 0.1 mg/kg x _____kg = _____mg (max 07 mg/dose) IV x1.

Ketamine 1 mg/kg x _____kg = _____mg (max 07 mg/dose) IV x1.
May repeat x1 dose if patient still responsive to nailbed pressure after 1 minute.

INTRAVENOUS KETAMINE FOR PROCEDURES >10 MINUTES (FILL IN BELOW)

☐ **<5 YEARS OF AGE**

Glycopyrrolate 0.005 mg/kg x _____ kg = _____mg IV x1

Ketamine 1 mg/kg x _____kg = _____ mg (max 70 mg/dose) IV x1.
May repeat x 1 dose if patient still responsive to nailbed pressure after 1 minute.

Ketamine 100 mcg/kg/minx _____kg = _____mcg/min IV drip to be iniated immediately after ketamine bolus above. Dilute ketamine to 10 mg/mL for continuous infusion. Assess patient Q10min for response to nailbed pressure. Titrate ketamine drip as necessary between 50 -125 mcg/kg/min.

Notify anesthesia if ketamine continuous infusion exceeds 60 minutes.

☐ **≥5 YEARS OF AGE**

Glycopyrrolate 0.005 mg/kg x _____ kg = _____mg IV x1

Midazolam 0.1 mg/kg x _____kg = _____mg (max 07 mg/dose) IV x1.
May repeat x 1 dose after 60 to 80 minutes if sedation still needed.

Ketamine 1 mg/kg x _____kg = _____ mg (max 70 mg/dose) IV x1.
May repeat x 1 dose if patient still responsive to nailbed pressure after 1 minute.

Ketamine 100 mcg/kg/minx _____kg = _____mcg/min IV drip to be iniated immediately after ketamine bolus above. Dilute ketamine to 10 mg/mL for continuous infusion. Assess patient Q10min for response to nailbed pressure. Titrate ketamine drip as necessary between 50 -125 mcg/kg/min.

Notify anesthesia if ketamine continuous infusion exceeds 60 minutes.

Fig. 12.4 Ketamine protocol for those who have adequate intravenous access. The protocol is divided into procedures less than 10 min and procedures greater than 10 min. Within these subdivisions, the protocol outlines doses for children less than 5 years and children greater than 5 years [21]

Another study compared a combination of dexmedetomidine and ketamine to a combination of ketamine and propofol for cardiac catheterization. The dexmedetomidine group had increased recovery time and required more ketamine than the propofol-ketamine combination [45]. In this study, one group received a dexmedetomidine and ketamine combination (1 μg/kg over 10 min and 1 mg/kg respectively) followed by dexmedetomidine infusion of 0.7 μg/kg/h and ketamine at 1 mg/kg/h.

Pentobarbital

The superiority of pentobarbital over choral hydrate was evident in a study of over 1,400 patients where pentobarbital was associated with a decreased incidence of adverse events [19]. In this study, the dose of oral pentobarbital used was 4 mg/kg that may be supplemented at aliquots of 2 mg/kg every 30 min to a maximum dose of 8 mg/kg [19].

Although the relative safety of the drug has been demonstrated, the drug has a relatively long half-life ranging between 15 and 48 h [46].

Dexmedetomidine

Dexmedetomidine is a highly selective α2 adrenoceptor agonist that has sedative and analgesic effects [47]. It is unique in that it is FDA approved as a sedative and has been shown to induce non-REM natural sleep [48, 49]. A sedation protocol using dexmedetomidine was developed at Children's Hospital Boston for Computed Tomography (CT) imaging. Although dexmedetomidine does not have any contraindications, their protocol advocated relative contraindications which are based predominantly on medical conditions [33] (see Table 12.2).

Patients would receive an initial loading dose of 2 μg/kg IV dexmedetomidine over a 10-min period, with appropriate monitoring. Using the Ramsay Sedation Scoring System, the child would receive an additional bolus of 2 μg/kg IV over 10 min to reach a Ramsay Sedation Score (RSS) of 4. Once the child achieves this level of sedation, the sedation is maintained with an infusion dose of 1 μg/kg/h until the procedure is finished. The patient is then transported to a recovery area until discharge criteria based on a modified Aldrete score is achieved [33]. This protocol has a low incidence of adverse events. The success of this protocol led to an expanded use of the drug in Magnetic Resonance Imaging (MRI), but the doses were increased to a 3 μg/kg bolus over 10 min which could be repeated if the level of sedation was not achieved. This was followed by an infusion rate of 2 μg/kg/h for the duration of the MRI [34]. This high dose regimen was highly effective for completion of almost all MRIs. While use of high dose dexmedetomidine is associated with decreases in heart rate and blood

Table 12.2 Contraindications on the use of dexmedetomidine as outlined in the Children's Hospital Boston guidelines

Dexmedetomidine
Active, uncontrolled gastroesophageal reflux
Active, uncontrolled vomiting
Current (or within the past 3 months) history of apnea requiring an apnea monitor
Active, current respiratory issues that are different from the baseline status (pneumonia, exacerbation of asthma, bronchiolitis, respiratory synctitial virus)
Unstable cardiac status (life-threatening arrhythmias, abnormal cardiac anatomy, significant cardiac dysfunction)
Craniofacial anomaly, which could make it difficult to effectively establish a mask airway for positive pressure ventilation if needed
Current use of digoxin, beta blockers, or calcium channel blockers
Moya Moya disease
Nononset stroke

Source: From Mason et al. [33]. Reprinted with permission of Wolters Kluwer Health

pressure outside the established "awake" normal values, this deviation is generally within 20% and is not associated with adverse sequelae.

Dexmedetomidine sedation has probably revolutionized sedation for imaging studies primarily for its safety and recovery profile [34, 37, 50]. There has been a case report whereby a 21-month-old female received 60 times the intended dose without any harm to the patient [51]. When administered as a sedative by non-anesthesiologists, dexmedetomidine may be supervised by an anesthesiologist who is not in continuous attendance but who may in fact be directing multiple sedation events in contiguous locations.

Propofol

Propofol, as a sedation drug, is perhaps the most controversial sedative agent currently used. It is not Food and Drug Administration (FDA) approved as a sedative, but rather is considered an anesthetic agent [52]. Its controversy lies in its respiratory depressant and hemodynamic side effects. Therefore, it requires careful titration and monitoring during its use. The package insert specifies that its use be restricted to those who are able to administer general anesthesia. In April 2004, the American Association of Nurse Anesthetists and American Society of Anesthesia made a joint statement on the need for restricting the use of propofol [53]:

> Whenever propofol is used for sedation/anesthesia, it should be administered only by persons trained in the administration of general anesthesia, who are not simultaneously involved in these surgical or diagnostic procedures. This restriction is concordant with specific language in the propofol package insert, and failure to follow these recommendations could put patients at increased risk of significant injury or death.

This statement has created much controversy among many physicians, such as intensivists, emergency room physicians, gastroenterologists and pediatricians who indicate that this position statement significantly restricts the use of this drug. The American College of Gastroenterologists filed a petition to ask the FDA to remove the restriction as written on the propofol label [54]. However, the FDA denied the request. They concluded that:

> For general anesthesia or monitored anesthesia care (MAC) sedation, DIPRIVAN Injectible Emulsion should be administered only by persons trained in the administration of general anesthesia and not involved in the conduct of the surgical/diagnostic procedure [54].

While these concerns over the safety of propofol for use by nonanesthesiologists continue, it appears that the controversies surrounding use of propofol by nonanesthesiologists may be unfounded. A review of prospectively collected data on approximately 49,000 propofol sedations by both anesthesiologists and nonanesthesiologists showed a low incidence of adverse outcomes [55]. "Nonanesthesiologists" included advanced nurse practitioners, pediatric nurses, physician's assistants, emergency physicians, pediatric intensivists, and radiologists. At least 48 and 36% of the sedations were performed by intensivists and emergency physicians, respectively. It was, however, interesting to note that anesthesia-related services using propofol were associated with fewer adverse events than nonanesthesiology providers [55]. A report of 25,433 propofol sedations to children by emergency medicine physicians, most for radiological imaging studies, demonstrated a 2.28% incidence of serious adverse events [56].

Nonetheless, the proliferation of use of propofol by anesthesiologists (and nonanesthesiologists alike) shows that it is a remarkably versatile drug to use for sedation. There are several advantages in the use of propofol: a rapid onset of action, it is easily titrable, and it allows a rapid recovery. Despite its lack of a reversal agent, propofol's duration of action is short. In addition, it has antiemetic properties. However, it has serious cardiac and respiratory morbidity and mortality risks and should only be used with appropriate training and monitoring. Sedation can be performed with this drug without compromising respiratory drive by appropriately titrating the agent. However, since it has no analgesic effects, there may be a need for appropriate concomitant analgesic agents. The combination of propofol-ketamine or propofol-fentanyl has been described previously and can be safe and effective [43].

Nursing Delivered Propofol

Nursing Delivered propofol has been controversial because its use needs to be restricted according to governing bodies such as the ASA and the Food and Drug Administration; both of which have issued statements that it should only be used by professionals trained in performing general anesthesia [53, 57]. The 2010 CMS amendment to the Hospital Anesthesia Services Interpretive Guidelines reflected these underlying concerns and was subsequently revised again [32]. These CMS guidelines were again revised in January 2011 in the PUB 100-07 State Operations Provider Certification which revises Appendix A for various provisions of 42 CFR 482-52 concerning anesthesia services [58]. These revisions were made in response to feedback from practitioners. Important changes in these guidelines stem from the CMS acknowledgement that the individual hospitals may establish their own policies and procedures with respect to the qualifications of analgesia providers and the clinical situations which distinguish anesthesia from analgesia. The policies must follow nationally recognized guidelines and can include guidelines of one or more specialty societies.

The University of Iowa has developed and implemented a unique propofol-delivered sedation program under the direction of the Department of Anesthesia. This program, initiated in 2008, is an example of a carefully designed and supervised model of propofol administration by registered nurses (RN). The history of the program is important and will be detailed below. The chronological retelling of the history illustrates not only the politics, but also the evolution of the program. The original premise of our consideration for use of propofol was that these RNs would always be carefully supervised by an anesthesiologist, and they would be trained to possess the airway skills necessary for deep sedation. The training program already emphasized the need for advanced airway training, which included the use of rescue devices such as a laryngeal mask airway. We also took into account the skills of the nurses, the type of procedures, the duration of the procedures, and the location of the procedures as a preamble to initiation of propofol sedation. At the inception of the program, propofol was not introduced and would not be considered until the nurses acquired experience with already established sedation protocols using pentobarbital, ketamine, midazolam, and fentanyl; most of which were protocols developed at Children's Hospital Boston [20, 21]. In the meanwhile, the Iowa Board of Nursing, proactive to rumors of possible propofol delivery by RNs to nonintubated patients, issued a statement: propofol could not be administered by nurses in the state of Iowa except on intubated patients in the Intensive Care Unit (ICU) and similar settings. Nurse anesthetists had already voted against RN administered propofol and the Board followed with a position paper after voting "to find that it is not within the scope of practice of the registered nurse to administer Propofol (Diprivan) during operative, invasive and diagnostic procedures in any type of health care setting effective December 1, 2007" [59]. Plans and education for RN-administered propofol at University of Iowa were subsequently aborted.

Our nurses, in the interim, continued to acquire sedation experience with drugs such as ketamine, pentobarbital, fentanyl and midazolam, as well as dexmedetomidine. The Pediatric Gastro-Intestinal Services team preferred propofol over ketamine, fentanyl, and versed combinations because there was a shorter recovery time and lower incidence of nausea and vomiting (despite pretreatment with anti-emetics). Physicians (including representation from our Department of Anesthesia), advanced nurse practitioners, and registered nurses returned to the Iowa Board of Nursing in 2008 and made a strong case for the negative impact on patient care caused by propofol restrictions [60]. The Iowa Board of Nursing subsequently rescinded the rule of restriction for the use of propofol by RNs [60].

Immediately after the rule was rescinded in September 2008, we initiated training of our RNs on the use of propofol for sedation purposes. The nurses already understood the use of End Tidal CO_2 monitoring in addition to other standard monitoring modalities. They also understood the importance of a defined, structured, propofol protocol which was founded on published reports of successful drug doses and combinations [41, 61].

Children < 10 years of age: Propofol-Ketamine Infusion

- Midazolam: 0.1 mg/kg IV - (Max 2 mg) Use as needed for anxiety
- Glycopyrrolate: 0.005 mg/kg IV (Max 0.2 mg) use for all Propofol procedures
- Initial P/K bolus: 0.5 mg/kg/0.05 mg/kg IV - (may be repeated Q30 seconds till Riker 3)
- Infusion P/K: 100-125 mcg/kg/min (use on procedures >20minutes)
- AS needed: Bolus Propofol 0.5mg/kg IV prn Q30 seconds until Riker 3

(HOLD Boluses and/or infusion if RR less than 20% of baseline or BP MAP less than 20% of Baseline)

Children > 10 years of age: Propofol Infusion ONLY

- Midazolam: 1-2 mg IV (Max 2mg) Use as needed for anxiety
- Initial Propofol bolus: 0.5 mg/kg IV – (May be repeated Q30 seconds until Riker 3)
- Infusion Propofol: 150 mcg/kg/min (use on procedures >20minutes)
- As needed: Bolus Propofol 0.5mg/kg IV prn Q30 seconds until Riker 3

(Hold Boluses and/or infusion if RR less than 20% of baseline or BP MAP less than 20% of Baseline)

FLUID BOLUS: 10-20 ml/kg IV for all children (discuss with Anesthesiologist for children with congenital heart disease before bolus is administered)

P:K= 10:1 :Preparation of ketamine propofol mixture:

50ml Propofol vial = 500 mg of 10mg/ml: TAKE 50ml of propofol

5ml Ketamine vial = 500mg of 100mg/ml: TAKE 0.5ml of ketamine

P-K total volume = 50 ml + 0.5 ml = 50.5 ml →

P-conc. = 9.9mg/ml in mixture of propofol and ketamine

K-conc = 0.99 mg/ml in mixture of propofol and ketamine

Fig. 12.5 University of Iowa: Nonanesthesiologist delivered propofol protocol

Children <10 years of age would receive a drug combination of propofol and ketamine in the ratio 10:1 up to a maximum dose of 125 μg/kg/min. The ketamine was intended to provide some analgesic and propofol sparing effect. The protocol evolved after review of Outcome and Quality Assurance data. Ketamine was not an adjunct to propofol for procedures in children >10 years of age, for fear of hallucinations, nausea, and vomiting in that age group. Initially, the time interval between boluses was at 1 min intervals and was slowly reduced to 15 seconds after the nurses gained experience.

Propofol is now being administered using established protocols at the University of Iowa for endoscopies, bronchoscopies, and radiological imaging studies. Every patient is assessed and consented by the anesthesiologist. (The sedation nurse independently assesses the patient first and also discusses the sedation process.) Each day an anesthesiologist is assigned to supervise sedation and has no concomitant operating room obligations. The anesthesiologist is usually present during the initial phase of propofol sedation and will remain immediately available for the rest of the case. After the procedure is complete, the propofol infusion is discontinued and the patient is transported on monitors (including end tidal CO_2) to the recovery room. The recovery nurses are allowed to discharge the patient based on preestablished discharge criteria. The anesthesiologist will see the patient before discharge if there were any issues during sedation or if a concern was brought up by a recovery nurse.

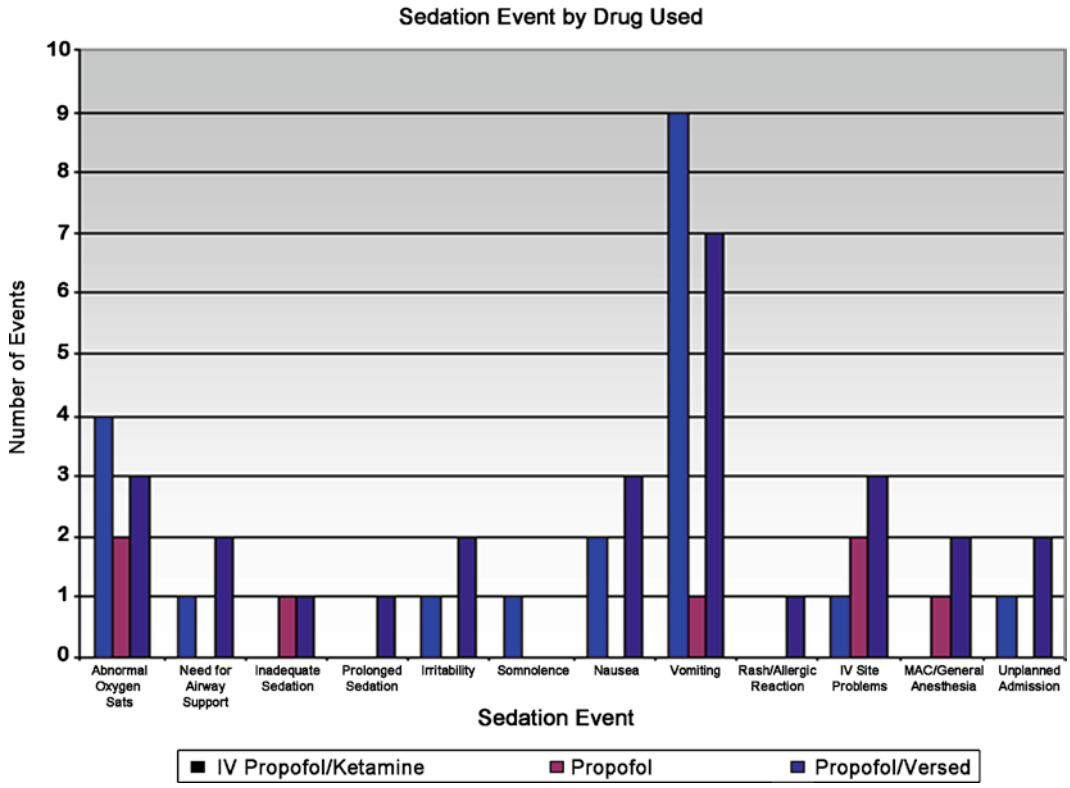

Fig. 12.6 This graph outlines the sedation related events associated with the use of propofol alone and in combination with ketamine and versed. The events shown include side effects of drugs such as nausea and vomiting, airway associated problems such as abnormal oxygen saturations, quality of sedation such as inadequate sedation, IV site problems, and adverse events such as unplanned admissions. (University of Iowa Propofol Sedation Program. Incidence of Adverse Events $n = 1{,}500+$ sedations.) Created by Joss J. Thomas, MBBS, MPH; University of Iowa Hospitals and Clinics, Iowa City, IA

The anesthesiologist can supervise multiple sedations in contiguous locations at the same time. However, the anesthesiologist can also restrict the volume to one sedation at a time, if it is deemed necessary for safety. For example, if a medically challenging patient needs closer supervision and monitoring, the schedule is modified to enable the anesthesiologist to only supervise this pre-sedation. A propofol template order set has been created on the electronic medical record system and these orders are signed by an anesthesiologist. The sedation nurses retrieve the propofol from the the operating room pharmacy. The order set is exclusively used by the sedation team (see Fig. 12.5).

Since October 2008, there have been over 1,500 propofol sedations. Initial unpublished data indicates a low incidence of adverse events (see Fig. 12.6). There were three unanticipated hospital admissions. The first admission was a 6-year-old male who had multiple oxygen desaturations to the high 80's during an endoscopy and was admitted to the hospital for observation. The second case was a 4-month-old male who suffered protracted coughing episodes during G-J tube placement. He was transferred to the pediatric intensive care unit (PICU) intubated, and subsequently extubated with no further issues. Finally, a 35-month-old male desaturated to the low 80's during upper endoscopy and required positive pressure bag-mask assisted ventilation. He was admitted to PICU and was intubated. Follow-up revealed that this child had an unrecognized upper airway condition which, had it been noted on the prescreening evaluation, would have contraindicated the sedation. This experience reiterates the

importance of careful screening, protocols, and guidance as anesthesia develops sedation programs for nonanesthesiologists.

Conclusion

An anesthesiology-directed sedation team can provide a safe and efficient sedation service. While it would be ideal that anesthesia personnel are always available to provide such a service, the reality is that the priority for anesthesia resources remains with the operating room. Very few centers have adopted a model such as an anesthesia-supervised nurse sedation team and, unfortunately, anesthesia's presence outside the operating room as a sedation provider remains limited. In response to this shortcoming, various other specialties, such as gastroenterologists, emergency room physicians, pediatricians and radiologists, have taken up the responsibility to provide this service. It is important to recognize that the Department of Anesthesia still has to play an integral role in monitoring sedation practices in an institution and developing the standards of training, monitoring and credentialing nonanesthesiologists to provide sedation services. The Centers for Medicare and Medicaid (CMS) recently revised the guidelines regarding delivery of anesthesia services [32]. For the first time, deep sedation was included as part of anesthesia services. CMS proposed that there be a consolidation of anesthesia services:

> All services along the continuum of anesthesia services provided in a hospital must be organized under a single Anesthesia Service [32].

Apropos to these guidelines, the Department of Anesthesia may need to play a more active role in the management and oversight of sedation services throughout the institution.

Case Studies

Case 1: Bronchoscopy with Sedation

A 5-month-old female weighing 7 kg (52% of growth percentile based on length-for-age) is being evaluated by bronchoscopy for persistent cough and expiratory wheeze. The child was otherwise healthy, with normal baseline vitals and saturations of 99% on room air. She had coarse expiratory crackles on auscultation, but other systems were normal. The pulmonologist wanted to perform a dynamic airway evaluation as well as obtain a broncheoalveolar sample.

***Considerations*:** The very nature of patients who require bronchoscopy makes them more susceptible to airway- and respiratory-based problems. These patients have a respiratory status that is already compromised secondary to an airway problem, such as laryngomalacia. They are likely to have sustained an infection such as unresolved pneumonia or a persistent reactive airway. It is advised not to sedate a patient until 4–6 weeks after a pneumonia or pulmonary infection. However, such recommendations do not apply to patients who require a bronchoscopic evaluation. Therefore, these patients are at an increased risk of respiratory decompensation during sedation.

The level of sedation that is required changes with the indication for bronchoscopy. When a dynamic airway evaluation is required to assess for airway related problems, especially laryngomalacia, tracheomalacia, and bronchomalacia, a moderate level of sedation would allow the collapse of airways to be better visualized during vigorous work of breathing. Our pulmonologists have indicated that such potential diagnoses of airway problems can be missed when sedation is deeper than intended. On the other hand, a deeper level of sedation is ideal to attain bronchioalveolar lavage (BAL) samples. In some patients, a moderate level of sedation, followed by a deeper level of sedation, are both required as the pulmonologist performs a dynamic airway evaluation and subsequently obtains a BAL sample.

It has been our experience that changing the level of sedation can be a potential challenge during these procedures. Propofol allows rapid changes in depths of sedation with careful titration of the medication.

***The Sedation*:** The patient was sedated with propofol, at 0.5 mg/kg boluses, after an initial dose of glycopyrrolate at 0.005 mg/kg and midazolam at 0.1 mg/kg. Local topical lidocaine was applied by the pulmonologist based on a weight-based protocol.

During the procedure, the pulmonologist performed an airway evaluation with the bronchoscope via the nares. With moderate sedation, they noticed no laryngeal or tracheal malacia, but it was difficult to note if there was malacia in the right middle lobe. Mucous secretions were prominent in the right lobe and particularly in the right middle lobe. The patient was then deeply sedated during the BAL procedure with additional propofol. However, the patient required bag-mask ventilation for ten breaths after a bolus of propofol elicited a brief oxygen desaturation to the 70's during the BAL. The patient required CPAP for approximately 10 min after the procedure (for persistent desaturations to the 80s without CPAP). This was likely due to possible atelectasis post-procedure and perhaps also related to sedation. The patient recovered uneventfully with saturations of 97–100% on room air within 4 h. An aggregate total of 26 mg of propofol was administered to the child. The child was discharged with a working diagnosis of inflammatory airway disease of unknown etiology.

Case 2

A 4-year-old male with a left suprarenal neuroblastoma, which was metastatic to multiple locations including the right maxilla and orbit, requires a surveillance scan under sedation. He had undergone multiple rounds of chemotherapy and resection of his left adrenal gland, and had subsequently undergone two stem-cell transplants and chemotherapy with thiotepa and cyclophosphamide. Radiation therapy was complicated by renal insufficiency. We were consulted to help with sedation for a surveillance scan, which included a chest/abdomen/pelvis CT and a whole body nuclear bone scan. The child has had multiple imaging studies done before, and it was necessary to use a nasogastric tube for oral contrast since he refused to drink any medication or fluids during earlier imaging procedures at the hospital.

***Considerations*:** He would need to have an intravenous line placed for intravenous fluid hydration and intravenous contrast prior to the scan. A nasogastric (NG) tube would need to be placed for oral contrast. The additional comorbidity of renal insufficiency necessitated using a radio contrast-induced nephropathy prevention protocol that included appropriate hydration with fluids and bicarbonate intravenous drip for renal protection prior to, and immediately after, the intravenous contrast load required for chest CT imaging.

Further preparation for the nuclear scan indicated that there would be at least a 2 hour waiting time, during which the child need not be sedated. During this period he would get adequate hydration and a bicarbonate-based infusion.

***The Sedation*:** The child and parents were habituated to receiving intramuscular chemotherapy and requested this route of administration for sedation. A combination of 0.1 and 5 mg/kg of versed and ketamine respectively were administered intramuscularly. The child was adequately sedated for placement of the NG tube, intravenous line, and oral contrast. The child was allowed to wake up after oral contrast was given. After about 2 hours, the child was re-sedated using propofol infusion at 125–150 μg/kg/min, and the CT scan and bone scan were completed

without incident. While an intramuscular injection of sedation medications is not routine for patients who require oral contrast imaging studies, it was necessary to tailor a regimen that would facilitate the process of attaining good imaging studies while keeping the child comfortable. In such situations, eliciting the help of parents to assist with the administration of medications is sometimes necessary. The option of general anesthesia has been proposed as an alternative to the sedation, but since this procedure was likely to be repeated every 3–6 months, the parents preferred sedation.

Case 3

Three-year-old female with a past medical history positive for tracheomalacia, follicular bronchitis, subglottic stenosis, and esophageal reflux, needed a pH impedance probe placed by the pediatric gastroenterology team under sedation.

Patient was diagnosed with esophageal reflux since she was 3 weeks old. She had a persistent cough. She developed croup twice, and was diagnosed with laryngomalacia and follicular bronchitis.

***Considerations*:** The anesthesia team was concerned with her respiratory status and tracheal stenosis. She had been easily intubated with a size 4 ETT tube 2 months prior. The concern about aspiration risk was discussed, but the gastroenterology (GI) service following her indicated that this was chronic micro-aspiration. The patient's mother indicated that the child had no vomiting episodes. The placement of an impedance probe was a very short procedure routinely done under sedation. However, the anesthesiologist was concerned about the respiratory status since the patient probably had a low reserve (though her saturations were 99% on room air).

***The Sedation*:** After having discussed the concerns with the pediatric GI team, it was agreed to proceed with sedation. The anesthesiologist was at the bedside throughout. The patient was sedated with a propofol-ketamine mixture 10:1 ratio at 125 μg/kg/min with boluses at 0.5 mg/kg every 30 seconds as necessary. Using an Olympus Q180 video endoscope, the patient's esophagus was intubated without difficulty. The entire length of the esophagus was normal, without ulcerations, edema, erythema, or furrowing. The lower esophageal sphincter was normal. Upon entering the stomach, normal gastric mucosa was seen without erythema, ulcerations, or other lesions. The pylorus was normal and was easily traversed to enter the duodenum where, again, normal mucosa was visualized, with normal villi and no ulcerations or other abnormalities.

Following attempted placement of the pH impedance probe, the patient had a brief desaturation episode to the 30's after coughing for 30 seconds. She was mask ventilated after removal of the scope and probe. Her oxygen saturations responded immediately from low 30's to high 90's. It is likely that the impedance probe may have entered the airway. Once the oxygen saturations stabilized, the impedance probe was replaced without difficulty. The rest of her hospital stay was uneventful.

***Summary Thoughts*:** This case would probably have benefited from general anesthesia with an endotracheal tube to protect the airway. Though the pediatric GI team routinely places these pH impedance probes under sedation, the probe can inadvertently enter the airway. This case highlighted different viewpoints of risk vs. benefit between specialties on issues such as aspiration risk. The consideration of an aspiration risk vs. potential edema and further comprise of an already stenosed airway secondary to intubation, persuaded the anesthesiologist to

maintain spontaneous ventilation and avoid endotracheal intubation. However, the probability of the impedance probe entering the airway, even in good hands was probably not recognized as a concern. The pediatric GI team indicated that it is very rare for them to enter the airway because it is done under direct visualization with the scope.

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