were older and healthier. Nearly 80% of the events presented initially as respiratory compromise. We interpreted most of the subsequent unacceptable outcomes as the result of failure to rescue the patients.[2,3] Inadequate resuscitation contributed to adverse outcomes more frequently in nonhospital-based venues.

The purpose of the current analysis is to examine the relationship between medication-related factors and the adverse events reported above. Specifically, we examined particular drugs and drug classes, routes of administration, medication errors and overdoses, drug combinations and interactions, the number of medications administered, venues of drug administration and of the adverse event, practitioners, and patterns of drug use.

METHODS

Case reports were obtained from a variety of sources including: the Food and Drug Administration adverse drug reporting system via the Freedom of Information Act, the US Pharmacopoeia, and a survey of pediatric anesthesiologists, pediatric intensivists, and pediatric emergency medicine specialists who were all fellows of the American Academy of Pediatrics (AAP).[1] To focus specifically on medication-related issues, we recorded: patient weight, age, the doses of all sedative medications administered, their routes of administration, the class of practitioner administering the medication, venue of its administration, the venue of the adverse event, and outcome (death, permanent neurologic injury, prolonged hospitalization without injury, or no harm). All cases were independently examined by each of 4 investigators (C.J.C., H.W.K., D.A.N., and J.A.W.) to attribute the probable causes of the adverse events.[1,4,5] Subsequently, all 4 investigators reached consensus on the contributory cause(s). Data were analyzed for each drug, then further examined by combining them into classes of drugs, eg, opioids, benzodiazepines, barbiturates, sedatives, intravenous (IV) anesthetics, local anesthetics, and inhalation (INH) anesthetics. Maximum recommended doses for each medication were derived from the US Pharmacopoeia Dispensing Information book,[6] the *Physician's Desk Reference*,[7] or the *Children's Formulary Handbook*.[8] An overdose was defined as ≥1.25 times the maximum recommended dose. For chloral hydrate, the maximum dose was 100 mg/kg up to 2 g (see "Appendix"). Nitrous oxide and/or halothane were considered sedating drugs if administered at the time of the event; local anesthetics were not considered sedating medications.

Statistical Analysis

Descriptive analyses were conducted for patient demographics, outcomes, medical provider data, and venue. Statistical comparisons consisted of standard t tests or nonparametric group comparisons (eg, χ^2 with correction for small numbers or Mann-Whitney U test). Each report was analyzed independently by 2 pediatric anesthesiologists, 1 pediatric intensivist, and 1 pediatric emergency medicine physician to attribute the probable drug related contributory causes of each adverse event. This removed any bias that might have occurred with discussion among reviewers. Coded responses were sent to a statistical analyst who assessed level of agreement among the 4 reviewers using a 4-rater chance-corrected value (Sav; Sav is an index of agreement of nominal data among a group of raters).[1,9–12] After independent review, the 4 evaluating physicians rereviewed these documents and debated each report. Only cases in which consensus agreement was reached on probable drug-related contributory causes were accepted.[4,5] Disagreements were resolved on a case-by-case basis, and cases unrelated to procedural sedation, those relating to drugs no longer available, and those containing inadequate information for consensus agreement were eliminated from the database.

RESULTS

Four reviewers (C.J.C., H.W.K., D.A.N., and J.A.W.) independently examined 118 pediatric adverse sedation events. There were moderate levels of agreement among the reviewers, indicating that agreement was not by chance. There was also moderate κ-agreement for 2-rater combinations, demonstrating that medical specialty was not a notable influence on reviews. Twenty-three reports were excluded during the group review process because inadequate data were available for adequate evaluation ($n = 1$) or agreement could not be reached ($n = 1$); the case did not involve sedation for a procedure (eg, pain medication after a procedure; $n = 8$); alphaprodine was used for sedation (a drug no longer marketed; $n = 9$); or because the adverse event was unrelated to the sedation process ($n = 4$). The age distribution of the excluded cases was not different from the entire cohort. Ninety-five cases were accepted into the final database and were the basis for this analysis.

The children in the final cohort ranged in age from .08 to 20.0 years (mean ± standard deviation: 5.7 ± 5.5) and weight 2.5 to 75.0 kg (mean ± standard deviation: 21.9 ± 17.3 kg). Thirty-five children (37%) were not harmed by the adverse event or required some additional time in the hospital for treatment of an injury that did not result in permanent neurologic injury. The other 60 children (63%) had adverse outcomes defined as death ($n = 51$) or permanent neurologic injury ($n = 9$). Medication-related adverse events were allocated to the following categories: drug interaction ($n = 44$); drug overdose ($n = 39$ in 34 patients); premature discharge ($n = 11$); prescription/transcription error ($n = 9$); inadequate understanding of administered medications (pharmacokinetics or pharmacodynamics; $n = 8$); administration by unsupervised technician ($n = 4$); and prescriptions administered by a parent ($n = 2$). Some patients had more than 1 drug-related cause for the adverse event, eg, drug overdose and drug administered by a technician.

Patients were sedated with a wide variety of medications, most commonly opioids and benzodiazepines (Table 1). Some children received more than 1 drug from each class of drugs; for some patients the doses or routes of administration were not recorded. There was no relationship between negative outcomes and the general category of drug administered, ie, death and permanent neurologic injury were associated with all drug classes (P = not significant [NS]). Medications were administered by a number of routes: IV, oral (PO), intramuscular (IM), INH, submucosal (SM), rectal (PR), intranasal (IN), and subcutaneous (SC; Table 1). There was also no relationship between negative outcomes and the route of drug administration (P = NS).

Approximately one half of the patients were sedated by more than 1 medication, and often these were given by more than 1 route, eg, IM and INH, PO and IV, PO and INH, or IM and IV. There was an association between adverse outcome and the administration of 3 or more sedating medications (18/20 vs 07/70; $P = .006$, χ^2). In 5 patients, all of whom died, the number of medications administered is not known (Table 2).

Thirty-nine of 170 drug administrations where the

TABLE 1. Route of Drug Administration and Outcome*

Route	IV		PO		IM		PR		SC		IN		INH		SM		Unknown Dose or Route		Total	
Drug	D/I	T	D/I	T	D/I	T	D/I	T	D/I	T	D/I	T	D/I	T	D/I	T	D/I	T	D/I	T
Opioid	9	22	4	4	8	10			1	1							1	1	23	38
Benzodiazepine	9	23	4	4	1	1					4	4					3	4	22	37
Sedative/hypnotic	3	3	17	24	13	16	1	2											34	45
Barbiturate	10	10	2	2	1	1	6	7									1	1	20	21
Ketamine	0	2	0	3	1	3											1	1	2	9
Inhalation anesthetics													12	13					12	13
Local anesthetics									2	2					9	10			11	14
Totals	31	60	27	37	24	31	7	9	3	3	4	4	12	13	9	12	7	8		
Percent adverse outcome	52		73		77		78		100		100		92							

T indicates total for that class of drug and route of administration; D, death; I, permanent neurologic injury.
* One half of the children received >1 medication; in some patients the route of administration could not be determined.

dose was documented were given in ≥1.25 times the maximum recommended dose in 34 patients (23%). Twenty-four of the 34 patients (71%) who received an overdose died or had permanent neurologic injury; all 4 patients who received 2 drugs at an overdose died (2 dental, 1 radiology, and 1 emergency department venue). Table 3 shows the number of administrations, medications, and range of drug overdoses; none of the 39 overdoses (3 local anesthetic and 36 sedating medications) in 34 patients seemed to be a simple decimal place error, ie, there were no 10-fold overdoses.

Table 4 presents the range of drug doses as a fraction of the maximum recommended dose when administration of a single drug was associated with death or permanent neurologic injury. Single doses of chloral hydrate, methohexital, pentobarbital, thiopental, ketamine, and midazolam were administered by a variety of routes. Several of these deaths/injuries occurred despite the fact that the reported doses were within the recommended limits: methohexital (2), chloral hydrate (1), and midazolam (1).

Table 5 describes the use of drugs in hospital-based and nonhospital-based venues. The only suggested pattern of drug use with venue of sedation was that all administrations of nitrous oxide took place in a nonhospital-based venue ($P < .01$) and 8 of 9 ketamine administrations were in a hospital-based facility (one was in an unknown environment; P = NS).

Twelve patients, all <6 years of age, suffered the adverse event either at home ($n = 8$) or in an automobile ($n = 4$); 11 of these had an adverse outcome. Five had undergone or were scheduled for a dental procedure, 5 for radiologic procedures, 1 for audiologic testing, and 1 for circumcision in a pediatrician's office. Ten occurred after discharge and 2 occurred at home before the scheduled procedure. Seven of these 12 children had received 1 medication, 2 received 2 medications, 2 received 3 medications, and 1 received 4 medications. Chloral hydrate was the drug most frequently associated with an adverse event occurring at home or in an automobile ($n = 7$); in 5 cases it was the only drug administered. One of the 7 chloral hydrate associated events occurred at home before arriving at a radiology facility and was caused by a prescription error. In another case, the drug was administered at home but the death was discovered on the child's arrival at the health care facility. Three patients who received chloral hydrate died or suffered permanent neurologic injury after discharge from a nonhospital-based venue. The other fatal event before arrival at a medical facility was associated with administration of midazolam (0.5 mg/kg, PO) at home; this child was found dead in a car seat when the family arrived at the nonhospital-based venue. Other drug combinations associated with an accident after discharge from either a hospital or a nonhospital-based facility all involved IM administration of medications with long half-lives: meperidine, promethazine, and chlorpromazine (Demerol, Phenergan, and Thorazine [DPT]; $n = 1$); pentobarbital (8 mg/kg; $n = 1$); and meperidine and promethazine (DP; $n = 1$).

TABLE 2. Association Between the Use of Multiple Sedative Medications and Outcome*

Number of Medications	n	Death or Neurologic Injury	Prolonged Hospitalization /No Harm
1	45	24	21
2	25	13	12
3	15	13	2
4	4	4	0
5	1	1	0
Unknown	5	5	0
Total	95	60	35

* Note that 50% of children received >1 sedating medication.

Children sedated for dental procedures accounted for 32 events resulting in 29 patients suffering death or permanent neurologic injury (11 practitioners were oral surgeons, 17 were dentists with unknown training, 3 were pedodontists, and 1 was a nurse anesthetist supervised by a dentist). The only apparent difference in the pattern of drug class selection by dental practitioners compared with those performing other procedures was the use of nitrous oxide and the use of multiple sedating medications. Eight dental patients received 1 drug, 8 received 2, 10 patients received 3, 1 patient was given 4 drugs, 1 patient was given 5 medications, and in 4 the number of medi-

TABLE 3. Overdoses* Compared With Number of Administrations*

Drug	Total Administrations	Total Overdoses	Death or Permanent Neurologic Injury Associated With Overdose	Range of Overdoses as a Fraction of Maximal Recommended Dose†
Opioids	37	10	7	1.3–4
Benzodiazepines	33	4	3	1.5–4.62
Sedative/hypnotics	45	11	8	1.25–3.0
Barbiturates	20	7	6	1.32–6.0
Ketamine	8	4	1	1.54–4.14
Local anesthetics	14	3	3	2.06–3.5
Totals	157	39	28	

* Some patients received >1 drug in an overdose.[6,7,94]
† Overdose was defined as ≥1.25 the maximal recommended dose.

cations was unknown. A higher proportion of patients undergoing dental care received 3 or more sedating medications at the time of the severe adverse event (death/permanent neurologic injury), compared with all other specialties combined (11/28 vs 8/62). All 10 patients who received nitrous oxide were dental patients and 9 of these suffered a negative outcome. Drugs coadministered with nitrous oxide and associated with negative outcomes were thiopental (PR, $n = 1$), promethazine (PO, $n = 1$), meperidine (PO, $n = 2$ and IM, $n = 1$), diazepam (PO, $n = 1$ and IV, $n = 2$), chloral hydrate (PO, $n = 2$), and pentobarbital (PO, $n = 1$).

Specific Medications

Opioids

Thirty-eight patients received opioids; opioids were associated with death or permanent neurologic injury in 23 patients, while 5 had prolonged hospitalization without injury and 10 had no harm. Opioids were administered as the only medication in 4 patients, combined with another medication in 16 patients, 2 other medications in 13 patients, 3 other medications in 3 patients, and with 4 medications in 1 patient. Twenty-one patients received meperidine, 10 received fentanyl, 4 morphine, 1 pentazocine, 1 oxymorphone, and 1 nalbuphine.

Benzodiazepines

Thirty-seven patients received benzodiazepines; benzodiazepines were associated with death or permanent neurologic injury in 22 patients, while 8 had prolonged hospitalization without injury and 6 had no harm. Twenty-six patients received midazolam by a variety of routes (Table 1). Midazolam was administered as a single sedative in 7 patients, combined with another medication in 12 patients, combined with 2 sedating medications in 5 patients, and with 3 or 4 sedating medications in 2 patients. Twelve children who received midazolam suffered death or permanent neurologic injury. Four of these 12 patients received midazolam as the only sedative. In 2 of these 4 cases, infants received IV overdoses, while in one third the IV dose was not described. The fourth case was associated with midazolam (PO) and is described above. Ten patients received diazepam: 5 with 1 other medication, 3 with 2 other medications, and 1 each with 3 or 4 other medications. Nine of these patients suffered death or neurologic injury and 1 had prolonged hospitalization. One patient received lorazepam (IM) combined with rectal methohexital, each administered as an overdose. This patient suffered a respiratory arrest during the recovery period and subsequently died.

TABLE 4. Single Drug Administrations Associated With Death or Permanent Neurologic Injury

Drug	Route	n	Range of Dose (Percent of Maximum)
Chloral hydrate	PO	7	0.6–3.0
	PR	1	
Methohexital	IV	5	0.73–2.7
	PR	1	
Thiopental	PR	2	1.3–3.5
Pentobarbital	IM	1	1.3
Ketamine	IM	1	1.75
Midazolam	IV	2	0.64–2.7
	PO	1	
	IN	1	

Chloral Hydrate

Fifteen of the 20 patients who received chloral hydrate were undergoing dental or radiologic procedures. Thirteen of the chloral hydrate sedated patients died or sustained a permanent neurologic injury; 5 were dental patients, 5 undergoing radiologic procedures, 2 cardiology procedures, and 1 an audiology procedure. Chloral hydrate was the only medication administered in 7 patients, and in 6 it was combined with other medications. Of the 7 cases in which chloral hydrate was the only drug administered, 4 patients received an overdose; 2 received an unknown amount of drug (1 at home and the other in a hospital venue); and the seventh received a standard dose (60 mg/kg). In the 6 cases in which chloral hydrate was combined with other sedating medications, all doses were within recommended limits. Four of these patients were sedated for dental care: 2 events occurred in a nonhospital-based facility and 2 at home after the procedure. The other 2 were sedated for radiologic procedures: 1 event occurred in the automobile after the procedure and in the other the venue was unknown. One of the patients was known to have an unstable cervical spine. Other preexisting medical problems in the 13 patients who received chloral hydrate and suffered an adverse

TABLE 5. Distribution of Drug Use by Category and Venue*

Drug	*n*	Hospital-Based Venue (*n* = 43)	Nonhospital-Based Venue (*n* = 28)	Unknown Venue (*n* = 24)
Opioids	38	19	9	7
Benzodiazepines	37	18	9	9
Sedative/hypnotic	45	18	16	11
Barbiturates	21	4	8	9
Intravenous anesthetic (ketamine)	9	8†	1	0
Inhalation anesthetics	13	0	11‡	2
Local anesthetics	14	2	8	4

* Note that some patients received >1 medication making the totals greater than the number of patients. The route of administration was not available for all drugs.
† *P* = NS compared with nonhospital-based vneue.
‡ *P* = <.01 compared with hospital-based venue.

outcome (*n* = 1 for each) included: tracheomalacia, tracheostomy, congenital heart disease, Möbius' syndrome, pulmonary artery hypertension, neonatal apnea, and cerebral palsy with seizures. An additional child with undefined congenital heart disease died after receiving an unknown amount of chloral hydrate.

Barbiturates

Twenty patients received barbiturate sedation. Nineteen died or had a permanent neurologic injury. In 10 the barbiturate was the only medication administered, 4 received 2 sedating medications, 1 received 3 sedating medications, 4 received 4 sedating medications, and 1 received 5 sedating medications. One received both methohexital and pentobarbital. The venue of the accident was not described in 8, a hospital-based venue in 3, a nonhospital-based venue in 8, and 1 patient died at home after pentobarbital (8 mg/kg, IM). Eight patients were undergoing dental procedures, 7 radiologic procedures, 3 gynecologic procedures (therapeutic abortions), and 1 an interventional cardiology procedure. Underlying medical problems in these patients included: histiocytosis (1), craniosynostosis (3), asthma (2), and developmental delay (1). The 1 survivor suffered a respiratory arrest after an overdose of rectal thiopental.

Local Anesthetics

Four children received overdoses of local anesthetics. Three were undergoing dental care and received 2 to 3.5 times the maximal recommended doses of either mepivacaine (*n* = 2) or lidocaine (*n* = 1). The other patient was treated in an emergency department and received an accidental IV injection of local anesthetic that was within the maximum recommended dosing limits. Two children initially developed seizures and 2 respiratory depression. Three progressed to cardiac arrest; all 4 children died.

DISCUSSION

Our study demonstrates that children suffered drug-related adverse outcomes after administration of a wide variety of medications. The data suggest a relatively even distribution of adverse sedation events in children across the major drug classes (opioids, benzodiazepines, barbiturates, and sedative/hypnotics). The observation that negative outcomes were associated with all classes of drugs and all routes of administration is clinically important because it points out that these negative outcomes occur not because of the drugs themselves but rather because of drug administration practices (drug combinations, errors, and monitoring standards). These practices likely reflect the skills (or lack of skills) and knowledge (or a lack of knowledge) of the individuals who administered the drugs for procedural sedation. Many events related to medication errors have been well-characterized. Lack of knowledge of the drug, lack of patient information, failure to follow procedures, transcription errors, faulty dose dispensing, inadequate monitoring, and a variety of other causes have all been described and many of these were evident in out database.[13–18] Children in particular seen to be vulnerable; methods for prevention of medication errors in this group have also been described.[19] The recent report from the Institute of Medicine has highlighted a number of initiatives that could be used to reduce medication errors.[20] Clearly the training, the understanding of the pharmacokinetics and pharmacodynamics of the drugs administered, and systems issues (such as drug limits, double-checking drug doses, computer checks of drug doses, improved patient informatics, the direct involvement of pharmacists, and limiting the medications used for certain types of procedures) are potentially important mechanisms for reducing medication errors.[20–32]

Our observations are consistent with these and other reports concerning adverse drug events and medication errors. However, a number of adverse outcomes were related to systems issues, such as inadequate monitoring, lack of skills in cardiopulmonary resuscitation, inadequate recovery procedures, and others causes unrelated to the drugs administered. In addition, nearly one half of the adverse outcomes occurred in nonhospital-based facilities, where the usual hospital-based safety net of state-mandated regulations does not generally apply. Unfortunately there is no way of knowing the actual incidence of these sedation/medication-related events because these were voluntary reports and the data were collected retrospectively. However, it is very likely that the cases that we collected represent a gross underreporting especially because such reports are often used as a tool for measuring hospital/

physician/organizational performance.[33–40] We agree with the Institute of Medicine report which suggests the need for a national mandatory reporting system that would be "afforded legal protections from data discoverability... devoted to analyzing and understanding the causes of errors to make improvements."[20] Other proposed initiatives include voluntary reporting systems such as the Joint Commission on Accreditation of Health care Organization's sentinel event program, the Food and Drug Administration's MedWatch program.[41,42] Such initiatives would help to focus on both drug-related and systems-related issues.

Our study found that there was no clear relationship between the route of administration and negative outcomes. The IV route was used most frequently and was the least associated with negative outcomes; however, compared with other routes of drug administration, the difference did not reach statistical significance. Several adverse events were successfully treated because of timely recognition and antagonism of drug effects. Although the data are somewhat soft, it suggests a possible advantage to the use of drugs that can be reversed if an adverse event should take place. Thus the use of an opioid or benzodiazepine alone or in combination with each other or combined with other sedating medications may be safer because at least one of the drugs has a specific antagonist that can reverse respiratory depression should it occur. The tendency toward a lower complication rate may also be related to the immediate availability of IV access for administration of resuscitative agents. Furthermore, we hypothesize that the tendency toward fewer adverse outcomes when medications are given intravenously may in part be related to the ability of titrate drugs to affect afforded by this route. Single large doses are commonly used when drugs are administered by other routes and there is no titration of drug. Another possibility is that these patients were monitored more closely. These hypotheses should be investigated further in future studies.

In many states, dental office practice certificates are based in part on the route of drug administration. Because our data clearly demonstrate that the route of drug administration is unrelated to outcome, certification of office practice based on route of drug administration does not adequately protect patients. Instead, certification should be based on practitioners' training in the use of these medications and on their sedation assessment, airway management, and resuscitation skills. In addition, the 2 Current Procedure Terminology codes recently established for sedation reimburse practitioners according to the route of drug administration (sedation administered by the IV, IM, and INH routes is reimbursed at 1 rate; medications delivered by the PO, PR, and IN routes are reimbursed at another rate).[8] Many procedures are performed by physicians who are not trained to sedate children or who are uncomfortable sedating children. The new Current Procedure Terminology sedation codes only apply if the physician is performing the procedure himself or herself; this creates a disincentive for independent experienced physicians to participate in the sedation of children for other physicians. The cost to the practitioner or a medical facility to provide safe patient care during sedation for a procedure is related in part to the intensity and duration of the monitoring required. The routine use of an additional person whose only responsibility is to observe the patient certainly is an important factor in this cost. Reimbursement based on route of drug administration is fallacious and should be abandoned.

Many serious adverse events occurred when multiple drugs were administered despite the fact that each was administered in less than the maximum recommended dose. This suggests drug–drug interactions, the category most often associated with an adverse sedation event ($n = 44$) and a phenomenon that has been well-described in clinical studies.[43,44] Adverse outcome has been correlated with the number of drugs used to sedate children having computer-axial tomography scans.[45] Our study found a high association with death or permanent neurologic injury when 3 or more sedating medications were administered. Several children in our cohort suffered an adverse outcome even when appropriate doses of individual medications were administered in combination. This underscores the need for education regarding the potential for a greater than desired depth of sedation when combining sedating medications, even when each is administered within the recommended dosing limits. When administration of multiple drugs is planned, initial doses (mg/kg) should be lower than those for each drug given alone. Also, insertion of an IV line, perhaps after an initial nonparenteral dose of a drug, could facilitate titration of further sedative/analgesics.

Drug overdose was the second most common category of causes attributed to adverse sedation events (39 episodes in 34 patients). None of these involved a 10-fold overdose; this fact suggests that the errors were not simple multiplication/decimal point errors, but rather were caused by a lack of knowledge about drug dosing in children.[19] The 3 local anesthetic overdoses, an issue previously described in dental accidents, underscore the importance of double-checking all drug doses and of setting maximum mg/kg dose limits.[46,47] Perhaps some of these adverse events resulted from the lack of pediatric labeling for nearly every medication used for sedation, analgesia, and amnesia in children.[48–52]

Some children died or suffered permanent neurologic injury even when a single drug was administered in less than maximum recommended doses ($n = 4$). One of these was undergoing an echocardiogram and was sedated with chloral hydrate (60 mg/kg) by a technician; 1 was a 2-year-old sedated for a computer-axial tomography scan with methohexital (20 mg/kg, PR); another was a 3-year-old sedated by a parent with midazolam (.5 mg/kg, PO) who died in the car on the way to the dental office; and the fourth was a 19-year-old undergoing a therapeutic abortion in a clinic who received methohexital (<2 mg/kg, IV). Two of these 4 patients were not protected by the safety net of trained medical personnel. These cases illustrate the essential reason for

having sedation guidelines that admonish against administration of sedating/anxiolytic medications at home or by those not qualified to provide skilled observation and rescue should an adverse event occur. Sedation guidelines allowing preprocedural drug administration at home should be modified to eliminate such practices.

Adverse events occurred in both hospital-based and nonhospital-based venues because of prescription or transcription errors. In 1 case, the pharmacy filled a chloral hydrate prescription for tablespoons instead of teaspoons and at twice the concentration, resulting in a dose 6 times higher than that intended by the prescriber. These types of events illustrate the need to have the same standard of care and vigilance regardless of the route of drug administration, drug class, or the venue in which the drug is administered. Because medication errors may occur at any time and at the hands of very skilled practitioners, sedation areas and delivery systems should be designed to prevent the occurrence of any errors.[20,53,54] For example, procedure policies could require that orders and prescriptions clearly indicate the child's weight, mg/kg, and the total dose to be administered. Further titration of medications should be specified. Because practitioners use a small number of medications for their particular procedures, precalculated drug dosage cards like those commonly used in emergency and critical care settings would be relatively easy to create. Further engineering of injury proof delivery systems should be encouraged.

We were particularly surprised by the number of children who suffered a negative outcome after the administration of chloral hydrate. This drug is widely used for infants and toddlers and has a long-standing reputation as a very safe medication with minimal effects on respiration.[55–58] Chloral hydrate is often used as a single sedating agent or in combination with other sedatives, particularly for dental and radiologic procedures.[59–63] Thirteen of 60 cases resulting in death or permanent neurologic injury involved the use of chloral hydrate alone ($n = 7$) or in combination with other medications ($n = 6$). Adverse events after chloral hydrate included a number of medication-related factors: overdose, administration outside of the safety net of a medical venue (drug given at home), administration by nonmedically trained personnel (technician), and premature discharge from medical observation. One of the children who died after receiving an unintended chloral hydrate overdose was noted by the mother to have a rapid heart beat; this may have been a sign of chloral hydrate toxicity.[64–67] A technician rather than a medically trained individual supervised this child, and the potential clinical implications of the rapid heart rate were ignored. We do not know whether this child would have survived if a nurse or physician had intervened at that point. We suspect that the 2 children with congenital heart disease were vulnerable to the development of cardiac dysrhythmias. It is known that tonsillar and adenoidal hypertrophy and Leigh's encephalopathy are associated with airway obstruction in patients sedated with chloral hydrate.[68–70] Airway obstruction has also been associated with chloral hydrate administration to American Society of Anesthesiologists (ASA) physical status 3 children.[71] We do not know whether any of our cases had similar airway-related problems, but it was most disturbing to find that 1 child who died had received only 60 mg/kg of chloral hydrate, which is well within recommended dose limits. Our study clearly points out that chloral hydrate is no exception to the rule that medications capable of causing depressed levels of consciousness should never be administered by nonmedical personnel in a nonsupervised medical environment.[72]

Some children were injured in car seats on their way home after a procedure. A possible mechanism for the injury was the infant falling asleep with the rhythmic motion of the automobile and the head falling forward, thereby obstructing the upper airway. In the presence of residual drug effect, the child could be unable to arouse or unable to spontaneously reposition the head to relieve the airway obstruction. This sequence of airway obstruction and desaturation has been demonstrated in unsedated full-term neonates placed in car seats.[73] All 9 children who experienced an adverse event (8 of whom died or suffered permanent neurologic injury) at home or in an automobile after a procedure, received drugs known to have a long half-life in infants and children (chloral hydrate, promazine, promethazine, chlorpromazine, or phenobarbital [IM]; see "Appendix"). The active metabolite of chloral hydrate is trichloroethanol. In newborns the half-life of trichloroethanol is 27.8 ± 21.3 hours, whereas in toddlers it is 9.7 ± 1.7 hours.[74] Thus, although at the end of a procedure an infant or toddler may seem to have recovered from the sedative effects of chloral hydrate, residual drug, and active metabolite are still circulating and there is the potential for resedation once the child is no longer stimulated. Two other children who died or suffered permanent neurologic injury after discharge were sedated with the classic combination of DPT or chlorpromazine plus promazine. A pharmacodynamic study of DPT administered to pediatric patients in the emergency department has shown that it took a mean of 19 ± 15 hours for children who received this drug combination to return to normal behavior.[75] The half-life of a single dose of chlorpromazine in adults is 31 hours.[76] A half-life of 3.19 days has been demonstrated in newborns.[77] Children seem to have a shorter elimination half-life compared with adults (7.74 ± .65 hours) but this study was for IV not IM administration[78]; the pharmacokinetics are likely different after IM administration attributable to delayed absorption and depot effect. Promazine and promethazine have a half-lives of 12.65 ± 4.7 hours[79] and 10 to 14 hours in adults, respectively.[80] Promethazine also has age-related differences in pharmacokinetics. The half-life is shorter in children (7.1 ± 2.3 hours) after oral administration, compared with adults (20 ± 4.1 hours).[81,82] The pharmacokinetics of promethazine may also be different after IM administration because of delayed absorption and depot effects. Another drug associated with death after discharge was pentobarbital (8 mg/kg, IM). The

half-life of pentobarbital in children when administered intravenously is 25.5 ± 16 hours.[83] In many of these cases the known pharmacokinetic profile of these agents was apparently ignored because patients were discharged without complete recovery from sedation.

Our discovery of several patients with negative outcomes who received sedation with these medications is particularly relevant considering the widespread and long-time use of these medications for outpatient sedation for procedures, particularly for infants. There are minimal data regarding the pharmacodynamics of any of these drugs in children, especially how age, maturation of hepatic or renal function, route of administration, or enzyme inhibition might alter drug elimination. These cases clearly point out the need for very rigorous recovery procedures and discharge criteria. Our data suggest that children should rest/recover in a quiet monitored area after the end of the procedure, even if they seem to be awake immediately after it is completed. A step-down unit for further observation after discharge from a standard recovery area may be of value in children who have received sedative medications with long half-lives. Patient discharge must only be made by qualified personnel (nurse, physician, and dentist) and not by a technician. We would make the further suggestion that because of the very unfavorable pharmacokinetics and the known drug–drug interactions,[84–86] the combination of DPT should be abandoned, particularly for outpatient procedures and those performed in infants. Although DPT was useful in its time, many other better options are now available to practitioners.

Eight events, of which 5 resulted in death or neurologic injury, occurred in situations with clear evidence that the practitioners did not understand the pharmacology of the drugs that they had administered. Examples of this included several patients who developed chest wall and glottic rigidity after opioid administration, could not be ventilated or oxygenated, and died or sustained severe neurologic injury. Administration of naloxone may have been life saving. Another example was an attempt to reverse a chloral hydrate associated event with naloxone because the practitioner thought that chloral hydrate was an opioid. A third example was local anesthetic toxicity that resulted in seizures and arrhythmias that were then treated with additional lidocaine (IV). These cases clearly underscore the importance of intimate knowledge of the pharmacology and the pharmacodynamics of the medications used for sedation/analgesia. If a physician/dentist is going to administer any medication, they must understand the basic pharmacology of that drug and how to effectively manage expected drug-related complications.

We do not know the reason why dental specialists were disproportionately represented. In fact, we excluded 10 dental cases who died because 9 had received alphaprodine which is no longer manufactured and 1 received a drug (a transdermal fentanyl patch) for postdental surgery pain. Despite these exclusions this specialty had the highest representation with 29/32 suffering death or permanent neurologic injury. There was a very strong relationship of adverse outcomes with nonhospital-based facilities and with dental practitioners (n = 23). In some states, the category of sedation called Anxiolysis in the Dental Office Setting permits the prescription or administration of pharmacologic anxiolytics with concomitant use of nitrous oxide, without requirements for a special dental office anesthesia permit, advanced training, or pulse oximetry monitoring.[87] Seven patients who died or sustained permanent neurologic injury were given promethazine, diazepam, or chloral hydrate combined with nitrous oxide administered by nonanesthesiologists for dental procedures. Continuous monitoring of level of consciousness is particularly important, because many dental procedures in themselves compromise the airway: abnormal head and tongue positions; foreign materials (cotton and rubber dams); and the presence of blood, increased secretions, and exogenous water. Negative outcomes were also associated with the patient receiving 3 or more sedating medications. Dental practitioners accounted for the majority of patients who received 3 or more sedating medications and all the patients who received nitrous oxide. Nitrous oxide is generally considered to have minimal effects on respiration and consciousness. However when nitrous oxide is combined with any other depressing medication, even when the sedating medication is administered in standard doses, a state of deep sedation and/or general anesthesia may occur.[46,88–91] It is possible that drug–drug interactions, particularly with nitrous oxide, contributed to the adverse outcomes in the dental setting. The category of Anxiolysis in the Dental Setting, which allows anxiolytics to be combined with nitrous oxide without a requirement for monitoring, should be abandoned; this level of sedation requires the same training in airway management and monitoring as that required for deep sedation/general anesthesia.[72] In addition, the 1998 revision of the American Academy of Pediatric Dentistry (AAPD) sedation guidelines[92] deviates substantially from guidelines published by the AAP[72] and ASA.[93] The AAPD has divided the category of conscious sedation (equivalent to sedation/analgesia for the ASA guideline) into 3 categories. Conscious sedation level 3 is defined as a state of consciousness in which "repeated trapezius pinching or needle insertion in oral tissues elicits reflex withdrawal and appropriate verbalization (complaint, moan, crying)." The ASA document clearly states (and the AAP document will soon state) that reflex withdrawal is not considered to be a state of conscious sedation/ or sedation/analgesia but rather is consistent with a state of deep sedation/general anesthesia. These disparate definitions and approach to sedation monitoring and training need to be made consistent for all patients regardless of practice. We encourage all dental specialists to examine their practices and urge them to develop monitoring guidelines and training requirements similar to those adopted by the AAP and ASA.

CONCLUSION

Children have suffered adverse sedation-related outcomes with a variety of medications; adverse outcome does not seem to be related to drug category or route of drug administration. Even chloral hydrate administered well within the recommended maximal dose limits can cause serious morbidity and mortality. Monitoring of patients who receive this medication should be no less rigorous than that used for patients sedated with other sedative medications. Chloral hydrate should be considered a long-acting drug, capable of severe respiratory depression and/or airway obstruction. Medications with long plasma half-lives (chloral hydrate, promazine, promethazine, chlorpromazine, and pentobarbital) accounted for most of the deaths/injuries that occurred in automobiles or at home after a procedure. DPT should be abandoned for outpatients; a step-down unit for extended observation of outpatients treated with long-acting sedatives may be useful, especially for younger patients. This practice might be even more important for long-acting medications administered IM because a depot effect may occur that would prolong recovery even further. Prescription and transcription errors occur with sufficient frequency as to underscore the importance of a systematic approach to all patients who receive sedative medications, eg, setting mg/kg dose limits, using standardized dosing regimens, and double-checking all doses before their administration. Even standard and acceptable doses of drugs can cause significant morbidity and mortality if the patient is not properly observed. No child should be sedated without the safety net of skilled medical observation; the practice of administering sedating medications at home before a procedure is reckless, associated with the potential for disaster, and should be prohibited. A uniform standard of monitoring should be applied after administration of sedation medication, before, during, and after procedures. There must be no difference in the degree of vigilance related to the sedation or procedure venue or to the practitioner. Uniform monitoring guidelines should be applied by all practitioners and in all venues, where sedation is administered because the effects on the patient are the same regardless of who administers the medication or where it is administered. Office practice certificates should be based on training and expertise in pediatric resuscitation and with advanced airway management skills and not on route of drug administration. The category Anxiolysis in the Dental Setting should require advanced airway management skills, training in both pediatric basic and advanced life support, and appropriate patient physiologic monitoring. The definitions for the various levels of sedation should be unified among specialists. Standards of care, scope of practice, resource requirements, and reimbursement for sedation services should be based on the intensity of the monitoring required and of the duration of the procedure through recovery, not on the route of drug administration. Public agencies such as the Agency for Health Care Quality and Research, National Institutes of Health, National Patient Safety Foundation Research Program, and others should support further investigations into safe yet effective medications, combinations of medications, sedation techniques, training, and improved monitoring modalities.

APPENDIX. Drugs Used for Sedation—Range Recommended and Maximum (Underlined) Recommended Doses Used for This Analysis[6,7,94]

Drug	Route	Half-Life (T½ Hours)* Mean ± SD (Range)	Maximum Recommended Dose (mg/kg)
Fentanyl	IV	1.5 to 3[95–97]	0.00025–0.003
Morphine	IV	2.6 ± 1.7[98]	0.025–0.1
	IM	4.5 ± 0.3[99]	0.5–0.1
Meperidine	PO	6.98 ± 1.9[100]	0.5–2.0
	IV	3.0 ± 0.5[101]	0.5–2.0
	IM	4.5 ± 1.3[102]	0.5–2.0
Oxymorphone	SQ	3.4 (2.6–5.1)[103]	0.02–0.04
Pentazocine	IV	2.33[104]	0.1–0.5
Nalbuphine	IV	2.4 ± 0.4[105]	0.05–0.15
Diazepam	PO	44.5 ± 16.5[106]	0.1–0.4
	IV	20–66[107,108]	0.05–0.25
Midazolam	PO	1.7[109]	0.25–0.75
	IN	~2[110]	0.1–0.3
	IV	1.4–4[109,111,112]	0.025–0.2
Lorazepam		10.5 ± 2.9[113]	0.025–0.05
Chlorpromazine	IM	~31[76]	0.05–1.0
Promethazine	PO	7–14[80,81]	0.1–1.0
	IM		0.1–1.0
Promazine	IM	12.6 ± 4.7[79]	1.0–3.0
Hydroxyzine	PO	7.1 ± 2.3[82]	0.5–1.0
Diphenhydramine	IM	5.4 ± 1.8[114]	0.5–1.25
Chloral hydrate	PO	9.7 ± 1.7[74]	25–100
	PR		(or 2 g total) 25–100 (or 2 g total)
Thiopental	IV	6.1 ± 3.3[115]	0.5–5
	PR		15–30
Methohexital	IV	2.23 ± 0.78[116]	0.25–2.0
	PR	3.21 ± 1.25[116]	15–30
Pentobarbital	PO		2–6.0
	IM		2–6.0
Ketamine	PO		2–10
	IV	3.1 ± 1.6[117]	0.25–1.0
	IM		1–4.0
Mepivacaine	SC		6.0
Lidocaine	SC—with epinephrine		7.0
	SC—without epinephrine		5.0
Prilocaine	SC		7.0

The range of recommended doses is presented with the upper limits underlined. It should be noted that recommendations vary according to the needs of the specialist and patient.

* Note that these half-lives are for older children or adults when pediatric data are absent; the half-lives are likely to be considerably longer in neonates and infants. It should also be noted that the effective half-life (ie, the effect on the central nervous system) may last considerably longer than several serum half-lives. Children with impaired renal or hepatic function, those on vasoactive medications, and those receiving inhibitors of the cytochrome oxidase system (eg, erythromycin, calcium channel blockers, or protease inhibitors) may also have markedly prolonged elimination half-lives.[118–122]

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Angell R. Foreword. In: Strunk W, White EB. *The Elements of Style.* 4th ed. Allyn and Bacon; 2000

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Adverse Sedation Events in Pediatrics: A Critical Incident Analysis of Contributing Factors

Charles J. Coté, MD*; Daniel A. Notterman, MD‡; Helen W. Karl, MD§; Joseph A. Weinberg, MD‖; and Carolyn McCloskey, MD, MPH¶

ABSTRACT. *Objective.* **Factors that contribute to adverse sedation events in children undergoing procedures were examined using the technique of critical incident analysis.**

Methodology. **We developed a database that consists of descriptions of adverse sedation events derived from the Food and Drug Administration's adverse drug event reporting system, from the US Pharmacopeia, and from a survey of pediatric specialists. One hundred eighteen reports were reviewed for factors that may have contributed to the adverse sedation event. The outcome, ranging in severity from death to no harm, was noted. Individual reports were first examined separately by 4 physicians trained in pediatric anesthesiology, pediatric critical care medicine, or pediatric emergency medicine. Only reports for which all 4 reviewers agreed on the contributing factors and outcome were included in the final analysis.**

Results. **Of the 95 incidents with consensus agreement on the contributing factors, 51 resulted in death, 9 in permanent neurologic injury, 21 in prolonged hospitalization without injury, and in 14 there was no harm. Patients receiving sedation in nonhospital-based settings compared with hospital-based settings were older and healthier. The venue of sedation was not associated with the incidence of presenting respiratory events (eg, desaturation, apnea, laryngospasm, ~80% in each venue) but more cardiac arrests occurred as the second (53.6% vs 14%) and third events (25% vs 7%) in nonhospital-based facilities. Inadequate resuscitation was rated as being a determinant of adverse outcome more frequently in nonhospital-based events (57.1% vs 2.3%). Death and permanent neurologic injury occurred more frequently in nonhospital-based facilities (92.8% vs 37.2%). Successful outcome (prolonged hospitalization without injury or no harm) was associated with the use of pulse oximetry compared with a lack of any documented monitoring that was associated with unsuccessful outcome (death or permanent neurologic injury). In addition, pulse oximetry monitoring of patients sedated in hospitals was uniformly associated with successful outcomes whereas in the nonhospital-based venue, 4 out of 5 suffered adverse outcomes. Adverse outcomes despite the benefit of an early warning regarding oxygenation likely reflect lack of skill in assessment and in the use of appropriate interventions, ie, a failure to rescue the patient.**

Conclusions. **This study—a critical incident analysis—identifies several features associated with adverse sedation events and poor outcome. There were differences in outcomes for venue: adverse outcomes (permanent neurologic injury or death) occurred more frequently in a nonhospital-based facility, whereas successful outcomes (prolonged hospitalization or no harm) occurred more frequently in a hospital-based setting. Inadequate resuscitation was more often associated with a nonhospital-based setting. Inadequate and inconsistent physiologic monitoring (particularly failure to use or respond appropriately to pulse oximetry) was another major factor contributing to poor outcome in all venues. Other issues rated by the reviewers were: inadequate presedation medical evaluation, lack of an independent observer, medication errors, and inadequate recovery procedures. Uniform, specialty-independent guidelines for monitoring children during and after sedation are essential. Age and size-appropriate equipment and medications for resuscitation should be immediately available regardless of the location where the child is sedated. All health care providers who sedate children, regardless of practice venue, should have advanced airway assessment and management training and be skilled in the resuscitation of infants and children so that they can successfully rescue their patient should an adverse sedation event occur.** *Pediatrics* **2000;105:805–814;** ***sedation, adverse events, critical incident, medication errors, monitoring, guidelines.***

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The views expressed herein are those of the authors and not necessarily those of the Food and Drug Administration.

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ABBREVIATIONS. AAP, American Academy of Pediatrics; FDA, Food and Drug Administration; USP, US Pharmacopoeia; ASA, American Society of Anesthesiologists; SD, standard deviation.

Provision of safe sedation/analgesia for procedures on children requires skill and organization of resources to prevent severe negative patient outcomes because of adverse sedation-related events. In response to deaths associated with dental procedures,[1] the American Academy of Pediatrics (AAP) and the American Academy of Pediatric Dentistry published the first guidelines for caring for children requiring sedation for procedures.[2,3] Revision of these guidelines placed an emphasis on monitoring, including the routine use of pulse oxime-

try.[4,5] Despite these and other guidelines,[6–10] adverse outcomes from sedation-related events continue to occur. There remains disagreement regarding definitions for levels of sedation, the type and intensity of monitoring needed, the availability of emergency equipment, the number of individuals needed for observing sedated children, and the skills required of practitioners administering or supervising sedation.[11–14] A number of specialties have developed monitoring guidelines that differ from those of the AAP.[5,7,10]

There are clear similarities between the practice of anesthesiology and the administration of medications to children for sedation during procedures including the potential for an adverse outcome.[15–27] Adverse sedation events leading to death or injury are rare, data collection is difficult, and the fear of or actual litigation all contribute to the lack of published data on adverse sedation outcomes.[28] Investigators of anesthesiology-related mishaps have used critical incident analysis, a tool first developed by the aviation industry, to identify areas of concern.[21,29–38] Critical incident analysis is an objective evaluation of an event to discover what went wrong and why. This type of analysis is a useful tool in developing policy change to improve safety.

Critical incident analysis of adverse anesthesiology-related events involving thousands of patients has found that human error accounts for most mishaps.[15–27,39] Documented problems include: inadequate medical evaluation,[32,40] inadequate monitoring during or after the procedure,[41] inadequate skills in problem recognition and timely intervention,[32] and the lack of experience with a particular age patient or with an underlying medical condition.[32] The importance of an appropriately staffed and equipped recovery facility has also been documented.[42–45] The general availability of sophisticated monitoring equipment has helped to provide an early warning of developing adverse events. More importantly, critical incident analysis that defined the mechanisms of anesthesiology-related accidents led to the establishment of uniform nationwide specialty monitoring guidelines and practice parameters. A systematic approach to all anesthetized patients has led to a nearly 20-fold reduction in anesthesiology-associated morbidity and mortality for adults and children.[15,34,46–53]

The similarity of the administration of sedation to children undergoing procedures and the administration of anesthesia suggests that a comparable benefit in the reduction of preventable sedation-associated morbidity and mortality could result from a systematic critical incident investigation. Such an analysis has not been previously undertaken. Our study is intended to bring together a series of rare events from a variety of specialties and practice venues so as to identify areas of breakdown in the system that may have contributed to an adverse outcome regardless of the training or experience of the practitioner. Our database was collected to perform a systematic critical incident analysis of pediatric adverse sedation events so as to define strategies to reduce the risks inherent in the sedation of children.[32] We believed it important to have consensus agreement between 3 pediatric subspecialties (anesthesiology, critical care, and emergency medicine) so as to minimize bias related to reviewer practice.[36] We acknowledge that there are substantial limitations in this kind of data collection; however, despite these limitations, we believe that critical incident analysis of the information that is available can provide useful guidance in developing policies for prevention.

METHODS

Study Population

Through the Freedom of Information Act we obtained adverse drug reports received by the Food and Drug Administration (FDA) Spontaneous Reporting System from 1969 through March 20, 1996, concerning patients ≤20 years old. Manufacturers are required to report adverse drug events; physicians, pharmacists, health care professionals, and consumers may voluntarily contribute reports. One investigator (Dr McCloskey) examined 629 FDA pediatric adverse drug reports. Of these, 394 were excluded because they were duplicates or did not involve sedation for a procedure; 235 adverse drug reports (with all identifying data regarding hospital or practitioner names expunged) were forwarded for review. Pediatric adverse drug events reported to the US Pharmacopoeia (USP) were also obtained. A third source was case reports from a survey mailed to 310 pediatric anesthesiologists, 470 pediatric intensivists, and 575 pediatric emergency medicine specialists, all Fellows of the AAP. Several adverse sedation events were received anonymously. Reports from all sources with insufficient detail for interpretation, non-United States reports, cases involving alphaprodine (because this drug is no longer available), duplicate cases (eg, events reported to FDA, USP, and by the surveys) and cases related to general anesthesia or monitored anesthesia care provided by an anesthesiologist (because anesthesiology-related adverse events have had extensive systematic investigation) were excluded. This left 118 reports that formed the database for this analysis.

Data collected included the year of the incident, age, weight, gender, type of procedure, the venue in which the sedation drug(s) were administered, venue where the adverse sedation event took place, the medical specialty of the individual directing drug administration, the monitoring which was reported as being used, and the underlying medical conditions. Venue of sedation was assigned as hospital-based or nonhospital-based only when the records specifically described the venue. If that information was expunged or could not be ascertained from the documents, then the venue was classified as unknown. The number and type of medications administered, dose/kg, and route of administration were recorded. The American Society of Anesthesiologists (ASA) physical status was determined according to information within the reports (1 = a normal healthy patient, 2 = a patient with mild systemic disease, 3 = a patient with severe systemic disease, 4 = a patient with severe systemic disease that is a constant threat to life). Outcome was divided into 4 categories: 1) death, 2) permanent neurologic injury, 3) prolonged hospitalization without injury, or 4) no harm.

Statistical Methods

Descriptive analyses were conducted for medical provider data, patient demographics, venue, and outcomes. Statistical comparisons consisted of standard t tests or nonparametric group comparisons (eg, χ^2 with correction for small numbers or Mann-Whitney U). Critical incident analysis was used to determine contributing factors to the adverse events. Each report was first analyzed independently by 2 pediatric anesthesiologists, 1 pediatric intensivist, and 1 pediatric emergency medicine physician to attribute the probable contributory causes of each adverse event. This removed any bias that might have occurred with discussion among reviewers. Coded responses were sent to a statistical analyst who assessed level of agreement among the 4 reviewers using a four-rater chance-corrected value (Sav; Sav is an index of agreement of nominal data among a group of raters).[54–58] After independent review, the 4 evaluating physicians rereviewed the documents and each report was debated. Cases were only accepted when consensus agreement was reached on all probable contrib-

TABLE 1. Definitions and Examples of Categories of Probable Causes of Adverse Sedation Events

Probable Causes	Examples of Actual Reported Events
Drug-drug interaction—an event that was likely drug-related and for which a combination of drugs had been administered	"The 6-week-old infant received Demerol, Phenergan, and Thorazine for a circumcision and was found dead in bed 6 hours later"
Drug overdose—at least 1 drug was administered in a dose >1.25 times the maximum recommended dose. (*Physicians Desk Reference, United States Pharmacopoeia Drug Index, Children's Hospitals Formulary Handbook*)	"The child received 6000 mg of chloral hydrate"
Inadequate monitoring—this could have occurred during or after the procedure	"The child was not on any monitors"
Inadequate resuscitation—the records indicated that the individuals involved did not have the basic life support or advanced life support skills or did not appropriately manage the emergency. (Because this category required some degree of interpretation the reviewers were very conservative and if anything underestimated the actual number of these cases)	"The heart rate decreased from 98 to 80, the nurse anesthetist gave oxygen and atropine, the pulse decreased further into the 60s, the nurse anesthetist gave epinephrine, 4 minutes later the nurse gave Narcan, 3 minutes later the nurse gave Antilirium, 12 minutes later the ambulance was summoned, 10 minutes later the patient was intubated, the ambulance drivers found the child on no monitors, EKG revealed electromechanical dissociation, the patient was transported from the dental office to a hospital"
Inadequate medical evaluation—lack of evaluation or appreciation of how underlying medical conditions would alter the patient's response to sedative drugs	"A child was transferred from Mexico and received 60 mg/kg chloral hydrate for a cardiology procedure; respiratory depression and bradycardia were followed by cardiac arrest. Autopsy revealed a ventricular septal defect, pulmonary hypertension, and elevated digoxin levels"
Premature discharge—the patient developed the problem after leaving a medical facility before meeting recommended discharge criteria	"The child became stridorous and cyanotic on the way back to its hometown"
Inadequate personnel—either the medication was administered at the direction of a physician who then left the facility, or there were inadequate numbers of individuals involved to monitor the patient and carry out the procedure at the same time	"The physician administered the medication and left the facility leaving the care to a technician"
Prescription/transcription error—if patient received incorrect dose either because of a transcription or prescription error (pharmacy or nursing)	"The patient received tablespoons instead of teaspoons"
Inadequate equipment—if an emergency arose and the equipment to handle it was not age- or size-appropriate or not available	"An oxygen outlet was available but flow meter was not—only room air was available for the first 10 minutes"
Inadequate recovery procedures—this category included cases where there was not a proper recovery period, where no one was observing the patient after the procedure, or if an emergency occurred and the necessary equipment was not available	"If they made nurses stay after 5 PM they would all quit"
Inadequate understanding of a drug or its pharmacodynamics	"The patient was given 175 μg of fentanyl intravenous push; chest wall/glottic rigidity was followed by full cardiac arrest." Narcan or muscle relaxant were never administered
Prescription given by parent in unsupervised medical environment	The mother gave two prescriptions of chloral hydrate at home
Local anesthetic overdose—if child received more than the recommended upper limits or if an intravascular injection occurred	"A 22.7 kg child received 432 mg of mepivacaine for a dental procedure. Seizures were followed by respiratory and cardiac arrests"
Inadequate fasting for elective procedure	"The child received a bottle of milk prior to a CAT scan"
Unsupervised administration of a drug by a technician	The drug was administered by a technician, there was no physician or nurse in attendance
Unknown	The reviewer could not determine a likely cause of the event

utory causes (Table 1) and these were ranked in order of importance.[59,60] A primary, secondary, and tertiary cause was identified for each case; some cases had >3 contributory causes. Disagreements were resolved on a case-by-case basis; cases in which there was consensus that there was inadequate information to reach meaningful conclusions were eliminated. Only contributory causes agreed on by all reviewers were used in the final analysis. Inadequate resuscitation was determined from available information and defined as the global management of the resuscitation of an individual patient, ie, both basic and advanced life support exclusive of the availability of equipment.

RESULTS

Four reviewers (C.J.C., D.A.N., H.W.K., J.A.W.) independently examined 118 pediatric adverse sedation events. There were moderate levels of agreement among the 4 reviewers indicating that agreement was not by chance alone; there were also moderate κ agreement levels for two-rater combinations, demonstrating that medical specialty was not a notable influence on reviews. Twenty-three reports were excluded during the group reviewing process because the consensus was that there were inadequate data available to reach a conclusion or consensus agreement was reached that the case was not pertinent, eg, the event occurred after a surgical procedure. Of the 95 reports remaining, 57 adverse sedation events were from the FDA, 15 were reported by pediatric anesthesiologists, 12 by pediatric emergency medicine or intensive care specialists, 8 were anonymous, and 3 were from the USP. Fifty-one of 95 cases resulted in death, 9 in permanent neurologic

TABLE 2. Specialty Performing Sedation and Outcome

Specialty	*n*	%	Outcome	
			Death or Permanent Neurologic Injury *n* (%)	Prolonged Hospitalization Without Injury or No Harm *n* (%)
Total dental	32	33.7	29 (91)	3 (9)
Unknown dental specialty	16	16.8	14 (88)	2 (12)
Oral surgery	11	11.6	10 (91)	1 (9)
Pedodontist	3	3.2	3 (100)	0 (0)
General dentist	1	1.0	1 (100)	0 (0)
Dental nurse anesthetist	1	1.0	1 (100)	0 (0)
Unknown medical specialty	19	20.0	8 (42)	11 (58)
Radiology	15	15.8	11 (73)	4 (27)
Cardiology	5	5.3	3 (60)	2 (40)
Oncology	5	5.3	0 (0)	5 (100)
Emergency medicine	4	4.2	0 (0)	4 (100)
Gastroenterology	4	4.2	1 (25)	3 (75)
Unknown pediatric medical	4	4.2	2 (50)	2 (50)
Audiology	2	2.1	1 (50)	1 (50)
Gynecology	2	2.1	2 (100)	0 (0)
General pediatrician	2	2.1	2 (100)	0 (0)
Surgeon	1	1.0	1 (100)	0 (0)
Total	95		60	35

injury, 21 had a prolonged hospitalization without injury, and in 14 there was no harm. Ten cases were documented to have occurred before 1985 and in 6 the date was not available.

Responsibility for cases was distributed among a wide variety of specialties (Table 2). Thirty-seven patients were male, 33 female, and in 25 the gender was not described. The mean age and weight (±standard deviation [SD]) for the entire cohort was 5.7 ± 5.5 years (range, 1 month to 20 years) (Fig 1) and 21.9 ± 17.3 kg (range, 2.5 to 75.0 kg). In 71 out of 95 cases we were able to determine if the procedure was performed in a hospital-based facility (hospital, emergency department, or surgi-center) or a nonhospital-based facility (office or freestanding imaging facility) (Table A, Appendix 1). Patients cared for in a nonhospital-based versus a hospital-based venue were older (6.97 ± 5.75 years vs 3.84 ± 3.82 years; mean ± SD; $P = .015$), weighed more (26.53 ± 19.85 kg vs 16.47 ± 12.41 kg; mean ± SD; $P = .021$), and were healthier (lower ASA physical status; $P < .001$).

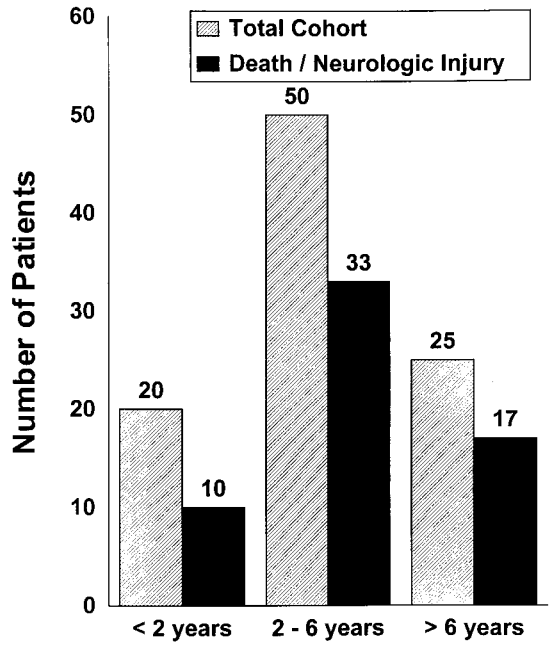

Fig 1. Distribution of cases by age. Note that the majority of patients were 6 years old or less but that there was no relationship between age and adverse outcome.

Table 3 presents the order of observed events as interpreted from the available information in the reports, eg, respiratory depression followed by bradycardia followed by cardiac arrest. Some indicator of respiratory compromise was the initially observed clinical event in >80% of patients regardless of the venue. However, there were significantly more cardiac arrests as the second (53.6% vs 14%, $P < .001$) and third (25% vs 7%, $P < .001$) events in the patients cared for in a nonhospital-based setting (Fig 2).

When the relative frequencies of causes judged to have contributed to adverse events were examined, drug-related events, inadequate monitoring, inadequate resuscitation, and documented inadequate medical evaluation were the most common. Inadequate resuscitation was judged to be substantially more common during management of nonhospital-based adverse sedation events (57.1% vs 2.3%; $P < .001$; Table B, Appendix 1). In addition, the outcomes of death and permanent neurologic injury occurred more frequently in patients cared for in a nonhospital-based facility (92.8% vs 37.2%; $P < .001$; Table C, Appendix 1; Fig 3).

There was a strong positive relationship between successful outcome (no harm or prolonged hospitalization without injury) in patients monitored with pulse oximetry and unsuccessful outcome (death or permanent neurologic injury) in patients whose reports specifically stated that no physiologic monitoring was used (χ^2; $P = .001$) (Table D, Appendix 1). This was also true when outcomes were rank-ordered by severity (Mann-Whitney U; $P = < .001$). Further analysis revealed that all 15 patients monitored with pulse oximetry in a hospital-based venue had either prolonged hospitalization without injury

TABLE 3. The Presenting Order of Observed Events*

Event	First			Second			Third		
	Entire Cohort	Hospital-Based	Nonhospital-Based	Entire Cohort	Hospital-Based	Nonhospital-Based	Entire Cohort	Hospital-Based	Nonhospital-Based
Respiratory depression	30.5	44.2	46.4	2.1	2.3	3.4	0.0	0.0	0.0
Respiratory arrest	43.2	27.9	28.6	14.7	14.0	25.0	2.2	2.3	3.6
Desaturation	5.3	9.3	3.6	10.5	16.3	4.0	0.0	0.0	0.0
Respiratory distress	2.1	2.3	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Laryngospasm	3.2	4.7	3.6	0.0	0.0	0.0	0.0	0.0	0.0
Cardiac arrest	8.4	2.3	10.7	30.5	14.0	53.6†	10.5	7.0	25.0†
Seizure	5.3	7.0	7.1	2.1	0.0	0.0	1.1	2.3	0.0
Unresponsive	1.0	2.3	0.0	2.2	2.3	4.0	1.1	0.0	0.0
Bradycardia	0.0	0.0	0.0	1.1	2.3	0.0	1.1	2.3	0.0
Unknown or no other event	1.0	0.0	0.0	36.8	48.8	10.0	84.0	86.0	71.4

* Each event is reported as a percent of the total number of patients in that category ($n = 95$ for entire cohort: for 24 the venue was unknown, 43 were hospital-based, and 28 were nonhospital-based events). Note that there was a higher incidence of cardiac arrest as the secondary and tertiary event in the nonhospital-based facilities; some patients only had 1 event.
† $P < .001$ compared with hospital-based adverse sedation events.

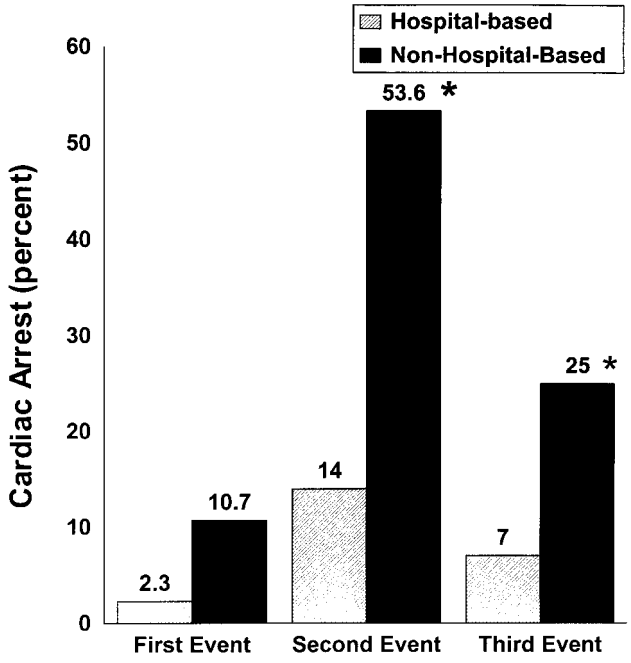

Fig 2. The sequence of presenting medical events revealed that a respiratory event was most common as the presenting event, however, in nonhospital-based facilities the incidence of cardiac arrest as the second or third event was significantly higher (*$P <$ .001). These data suggest that either there was a delay in recognition of the severity of the event or that the practitioners lacked appropriate skills in airway management and/or in cardiopulmonary resuscitation and failed to rescue the patient.

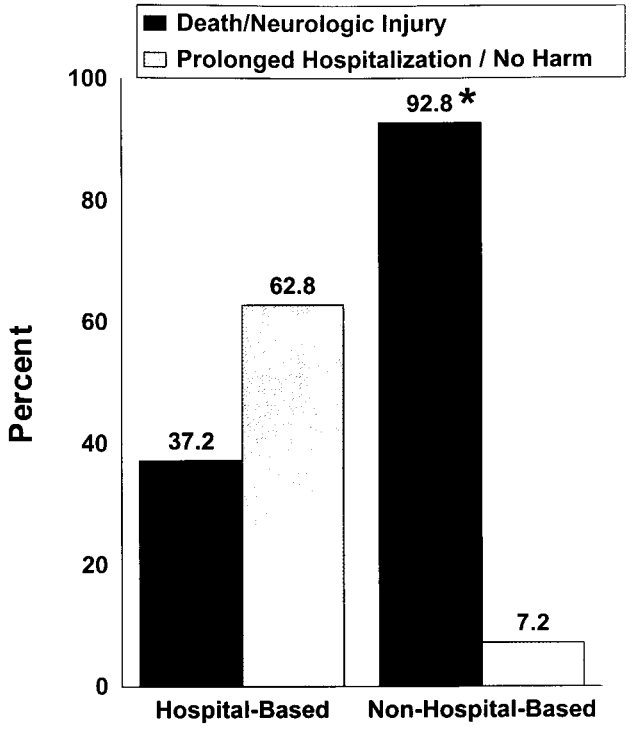

Fig 3. Outcome of adverse sedation-related events in children sedated in hospital-based compared with nonhospital-based facilities. Note that the outcome of death or permanent neurologic injury were significantly greater in nonhospital-based facilities (*$P <$ .001).

or no harm as the outcome. However, 4 out of 5 patients cared for in a nonhospital-based facility suffered death or permanent neurologic injury despite pulse oximetry monitoring ($P < .01$); the venue of care was not noted in 1 patient monitored with pulse oximetry. Data were inadequate to assess the role of other physiologic monitoring modalities.

DISCUSSION

There has been a dramatic increase in the number and complexity of procedures conducted in children; for many, compassion and successful accomplishment dictate the use of sedation/analgesia.[13,61–65] However, there are important safety concerns regarding the care rendered by a wide variety of practitioners with variable expertise and training in the administration of sedating medications. This concern is becoming more important because of the increasing number of procedures performed in nonhospital-based facilities by practitioners not necessarily trained in the care of children. We used critical incident analysis because this is the most efficient way of studying rare events to determine what went wrong and why. The intent of such analysis is not to be accusatory but rather to objectively evaluate the available data and interpret the events as a rational guide to systems changes that could prevent similar incidents in the future. Our study found that the most common issues judged to be associated with adverse sedation events were related to the effects of

sedating medications on respiration. Other factors included inadequate resuscitation by health care providers, medication errors, inadequate monitoring, and inadequate medical evaluation before sedation.

As expected, the first observed event was usually respiratory, regardless of the venue (~80%). However, in nonhospital facilities, the second and third medical events were 3 times more likely to be cardiac arrest. When a serious adverse sedation event occurred in a nonhospital-based facility, ~93% of children suffered death or permanent neurologic injury as the outcome, a 2.5-fold increase compared with children sedated in a hospital-based venue. These differences in outcome are even more clinically important because the nonhospital-based population was nearly twice as old and healthier (lower ASA physical status category). Inadequate resuscitation was judged to contribute to poor outcome 26 times more often in nonhospital-based facilities.

Although some adverse outcomes may occur despite supervision by highly skilled practitioners (nurse, physician, dentist) using optimal monitoring, our interpretation of the fact that the respiratory system was most often the first affected is that most of the poor outcomes could have been prevented with earlier recognition and appropriate intervention. The rank order of severity of adverse outcome and the incidence of death and permanent neurologic injury were significantly less in children monitored with pulse oximetry compared with those not monitored at all. A surprisingly large percentage of patients were apparently not monitored with pulse oximetry despite the wide availability of this technology after 1985. Of the patients known to have been monitored with pulse oximetry, 4 out of 5 patients sedated in a nonhospital-based venue suffered death or permanent neurologic injury, whereas none of the 15 patients sedated in a hospital-based venue and monitored with pulse oximetry had this severe adverse outcome. Thus, apparently despite the warning of a developing adverse event provided by pulse oximetry, these practitioners in a nonhospital-based venue were unable to perform adequate resuscitation. This marked difference in negative outcomes, despite the utilization of pulse oximetry in nonhospital-based facilities implies a failure to rescue the patient.[66] Our data suggest that there are a number of practitioners who sedate children for procedures who are unsafe because they either are not adequately vigilant during and after the procedure and/or they lack the skills to effectively manage the complications of sedating medications leading to respiratory or cardiovascular depression. These nonhospital-based events involved dentists, a radiologist, a general practice pediatrician, and a nurse anesthetist who was providing dental anesthesia but was not medically supervised by a physician. Delay in obtaining skilled help is another factor that may have played a role in the poor outcomes of patients sedated in nonhospital-based venues. In a nonhospital-based facility, often the only source of skilled help is the 911 emergency response system.

Our analyses revealed clear system breakdowns in a number of areas; most cases involved multiple breakdowns.[32,51,67–71] Some pediatric patients received sedating medications at home from a parent or at a facility from a technician rather than a nurse or physician and were thus left without the safety net of observation and monitoring by skilled medical personnel. Some practitioners discharged patients from medical supervision despite deep levels of residual sedation; some were sedated and discharged without ever being examined by a nurse or physician. Some practitioners did not provide adequate personnel to independently observe the patient, whereas others did not adequately monitor patients (particularly with pulse oximetry and an independent observer) during or after the procedure. Other practitioners apparently did not understand the basic pharmacology or the pharmacodynamics of the drugs administered, eg, the interaction of opioids and benzodiazepines on respiration or chest wall/glottic rigidity after intravenous fentanyl. Drug overdose was another prominent factor. Some practitioners did not recognize when they were in trouble and had exceeded their skills, ie, they did not cancel the procedure or call for additional assistance.

A disproportionate number of cases (32 out of 95) involved sedation/anesthesia for dental procedures (most in a nonhospital-based venue); a similar observation has been made in England.[53] This may reflect the fact that general dentists have little pediatric training, particularly in drugs used for sedation/analgesia, and a variety of other reasons.[14,72–74] The skills or training of the dental practitioners were not clear from the reports on which this study is based; 9 were identified as being oral surgeons who have the most training of the dental specialties for administering anesthetics/sedative agents. A possible systems issue related to dental care for children is that most insurance companies, health maintenance organizations, and state-funded insurance companies do not reimburse anesthesiology services for pediatric dental care, thereby forcing the dentist to provide needed sedation and monitoring while also providing dental care. The American Academy of Pediatric Dentistry is vigorously pursuing a campaign to obtain dental anesthesiology coverage in all 50 states but at the time of this writing only 21 mandate such coverage.(Personal communication, Ms Amy Johnson, American Academy of Pediatric Dentistry, September 9, 1999.) Even in states with dental insurance coverage for pediatric patients, it is generally limited to children with underlying medical problems (medical necessity) and not available for healthy patients. (Some states provide anesthesia coverage for children <5 years and for children who have behavioral management problems.) Our data clearly suggest that the majority of children undergoing dental procedures who suffered an adverse outcome did not have serious underlying medical conditions that would have added to risk. Our interpretation is that dental insurance coverage should be available for all children, not simply those with underlying medical conditions. Our data also suggest the need for improved training and monitoring standards for dental practitioners who care for children who do not need general anesthesia.

We recognize the limitations that the data collection methods place on our analysis. Reporter bias may certainly have been a factor. We also do not know the actual number of children with adverse sedation events who were rescued or the number of children sedated without an adverse sedation event. Our database likely represents only a small subset of adverse sedation events, because most of the reported cases resulted in death or permanent neurologic injury. The medical community is loath to publish such incidents because they are often the subject of litigation, they reflect negatively on the individual(s) involved as well as the institution in which they occurred, and because denial of responsibility for an adverse event is a common human trait.[32,67,68] There are no "flight recorders" to document the sequence of events leading to the rare occurrences of death or neurologic injury; prospective studies would require thousands of cases.[28,34,46,48,67–69,75] We also recognize that our interpretation of the events may have been influenced in part by knowing the outcome,[36] however, death and permanent neurologic injury are not soft endpoints and are unacceptable outcomes for healthy children sedated for procedures.

Despite the data collection limitations, important conclusions can be drawn from this critical incident analysis. The reports we obtained include all types of facilities from tertiary care centers to individual practitioner's offices. Our analysis suggests that the medical community has yet to adopt uniform guidelines of care for sedation for procedures as required by the Joint Commission on Accreditation of Healthcare Organizations and as recommended by a number of organizations.[4,7–10,76] Attention to systems issues such as a focused, goal-oriented history and physical examination before sedation; assurance of proper fasting; enforcement of minimum standards of training, monitoring, advanced airway management, and resuscitation skills; appropriate equipment and facilities, including recovery areas and discharge criteria would likely result in a marked reduction in sedation-related adverse events just as this systems approach has reduced anesthesiology-related morbidity and mortality.[21,27,30,34–38,46,48] Affecting outcome in nonhospital-based venues is complicated by the fact that these settings are often beyond the reach of the Joint Commission of Accreditation of Healthcare Organizations certification and guidelines, but rather fall under the purview of state regulatory bodies. Most states lack rigorous regulation of office-based sedation/anesthesia for children. Sedation for procedures in children share characteristics with the surgical suite, with general anesthesia,[21,32,34,52,77] with the aviation industry,[67] and other areas of the transportation industry where human error may have catastrophic consequences.[78,79] Guidelines and standards are applied by these industries and specialists to prevent a breakdown in systems designed to protect the traveler, worker, or patient. Similar protection should be provided to sedated children. Because sedating medications have the same effect on the patient regardless of where or who sedates the patient, it makes sense to have a rigorous and uniform approach.[80]

The safety issues observed in this critical incident study mirror adverse events associated with general anesthesia. Pulse oximetry is the single most helpful monitoring device for detecting impending life-threatening events.[41,81–97] Pulse oximetry, particularly the type that provides an audible change in tone as the saturation changes, should be required for every patient sedated for a procedure because it provides an early warning of developing oxygen desaturation to everyone present.[4,6–10,41] Most reports in our cohort did not indicate the use of pulse oximetry despite its general availability since 1985. Because >80% of events began with some compromise of respiration, other measures of monitoring the adequacy of respiration such as direct patient observation by an individual whose only responsibility is to monitor the patient may improve outcome. In addition, use of a precordial stethoscope and expired carbon dioxide monitor, when used as adjuncts to pulse oximetry, could aid in early recognition of a developing respiratory event.

Our analysis suggests that adverse outcome is not related to patient characteristics but rather to failure to rescue the patient from a developing adverse event.[66] It seems clear that timely recognition and intervention by individuals with appropriate airway management and resuscitation skills would likely have produced a different outcome for many if not most events in these patients. Our results strongly suggest that the systems issues described in the monitoring guidelines published by the AAP and the ASA, if rigorously followed in all venues and by all practitioners, would result in a marked reduction in serious sedation-related adverse events.[4,9] The striking difference in outcomes between hospital-based and nonhospital-based facilities suggests that children sedated in hospital-based facilities receive crucial benefit possibly because of superior resuscitation skills of providers in that venue and because help from other skilled health care providers is immediately available allowing for rescue. We do not know if an independent observer whose only responsibility is to monitor the patient was more likely to be used in a hospital-based compared with a nonhospital-based health care facility, but this may also have been a factor influencing outcomes. The third possibility is that the practitioners in a nonhospital-based venue simply lacked the skills for successful patient rescue. Our data strongly suggest that there is a need for more rigorous regulation as to the training and skills of practitioners who sedate children. Lastly, practitioners should recognize that "conscious sedation" is an oxymoron for many children <6 years old. Deep pharmacologic restraint is usually required to gain the cooperation of this age group; this increases the risk of an adverse respiratory event.[62,97–102]

CONCLUSIONS

This study—a critical incident analysis—identifies several features associated with adverse sedation-related events and poor outcome. An important association with outcome was venue. Adverse events that occurred in a nonhospital-based venue were far more likely to result in severe neurologic injury or

death than were adverse events that occurred in a hospital although patients cared for in nonhospital-based venues were generally older and healthier than those sedated in hospital-based facilities. Inadequate monitoring, especially failure to use or respond to pulse oximetry, was rated as a major factor contributing to poor outcome in all venues. Other issues rated as being a determinant of adverse outcomes were: errors in managing complications (failure to rescue), inadequate preprocedure medical evaluation, medication errors, inadequate recovery procedures, and the lack of an independent observer. Uniform, specialty-independent guidelines for monitoring children during sedation are essential; the same level of care should apply to hospital-based and nonhospital-based facilities. Pulse oximetry should be mandatory whenever a child receives sedating medications for a procedure, irrespective of the route of drug administration or the dosage. Age and size-appropriate equipment and medications for resuscitation should be immediately available in a designated crash cart, regardless of the location where the child is sedated. All health care providers who sedate children, regardless of practice venue, should have advanced airway management and resuscitation skills. Practitioners must carefully weigh the risks and the benefits of sedating children beyond the safety net of a hospital or hospital-like environment. Practitioners must understand that the absence of skilled back-up personnel could pose an important impediment to a successful outcome for the patient.

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APPENDIX

TABLE A. Venue of Sedation and Venue of Adverse Sedation Event

VENUE	Number Sedated in This Venue	Venue Where Event Took Place
Hospital or surgi-center	32	31
Emergency department	11	8
Nonhospital health care facility	28	22
Home	3	10
Automobile	0	4
Unknown venue	21	20

TABLE B. Categories of Causes Judged to Have Contributed to Adverse Sedation Events

Probable Causes of Adverse Events	Entire Cohort (n = 95)		Hospital-based (n = 43)		Nonhospital-based (n = 28)	
	n	%	n	%	n	%
Drug-drug interaction	44	46.3	19	44.2	18	64.3
Drug overdose	34	35.8	20	46.5	7	25.0
Inadequate monitoring	27	28.4	11	25.6	13	46.4
Inadequate resuscitation	19	20.0	1	2.3	16	57.1*
Inadequate medical evaluation	18	18.9	6	14.0	7	25.0
Unknown	12	12.6	4	9.3	1	3.6
Premature discharge	11	11.6	5	11.6	4	14.3
Inadequate personnel	10	10.5	4	9.3	5	17.9
Prescription/transcription error	9	9.5	4	9.3	1	3.6
Inadequate recovery procedures	8	8.4	4	9.3	2	7.1
Inadequate equipment	8	8.4	4	9.3	3	10.7
Inadequate understanding of a drug or its pharmacodynamics	8	8.4	2	4.7	2	7.1
Prescription given by parent in unsupervised medical environment	4	4.2	0	0	0	0
Local anesthetic overdose	4	4.2	1	2.3	3	10.7
Inadequate fasting for elective procedure	3	3.2	1	2.3	1	3.6
Unsupervised administration of a drug by a technician	2	2.1	1	2.3	1	3.6

* $P < .001$ Nonhospital-based versus hospital-based. Note that some patients had >1 cause for an adverse sedation event.

TABLE C. Outcome of Adverse Sedation Events in Hospital-Based Versus Nonhospital-Based Facilities (the Facility Could Not Be Determined for 24 Events)*

Outcome	Entire Cohort†		Hospital Facility		Nonhospital Facility	
	n	%	n	%	n	%
Death	51	53.7	13	30.2	23	82.1‡
Permanent neurologic injury	9	9.5	3	7.0	3	10.7‡
Prolonged hospitalization without injury	21	22.1	13	30.2	2	7.1
No harm	14	14.7	14	32.6	0	0
Totals	95	100	43	100	28	99.9

* Note that a significantly higher proportion of patients experiencing an adverse sedation event in the nonhospital-based venue suffered death or permanent neurologic injury as the outcome.

† The venue of sedation could not be determined for all patients.

‡ = $P < .001$ Compared with hospital-based sedation events.

TABLE D. Outcome From Adverse Sedation Events Where Pulse Oximetry Was Utilized Versus Those Events Where No Monitors Were Used

Outcomes*	Pulse Oximeter (n = 21)	No Monitoring (n = 18)
Death or neurologic injury	4	14†
Prolonged hospital stay or no harm	17	4

* Note that pulse oximetry was recorded as being used on 21 of 95 patients and that 18 reports specifically stated that no monitors were used.
† $P < .001$ compared with the use of pulse oximetry.

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Adverse Sedation Events in Pediatrics: A Critical Incident Analysis of Contributing Factors

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CLINICAL REPORT Guidance for the Clinician in Rendering Pediatric Care

American Academy of Pediatrics
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Guidelines for Monitoring and Management of Pediatric Patients Before, During, and After Sedation for Diagnostic and Therapeutic Procedures: Update 2016

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The safe sedation of children for procedures requires a systematic approach that includes the following: no administration of sedating medication without the safety net of medical/dental supervision, careful presedation evaluation for underlying medical or surgical conditions that would place the child at increased risk from sedating medications, appropriate fasting for elective procedures and a balance between the depth of sedation and risk for those who are unable to fast because of the urgent nature of the procedure, a focused airway examination for large (kissing) tonsils or anatomic airway abnormalities that might increase the potential for airway obstruction, a clear understanding of the medication's pharmacokinetic and pharmacodynamic effects and drug interactions, appropriate training and skills in airway management to allow rescue of the patient, age- and size-appropriate equipment for airway management and venous access, appropriate medications and reversal agents, sufficient numbers of staff to both carry out the procedure and monitor the patient, appropriate physiologic monitoring during and after the procedure, a properly equipped and staffed recovery area, recovery to the presedation level of consciousness before discharge from medical/dental supervision, and appropriate discharge instructions. This report was developed through a collaborative effort of the American Academy of Pediatrics and the American Academy of Pediatric Dentistry to offer pediatric providers updated information and guidance in delivering safe sedation to children.

abstract

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INTRODUCTION

The number of diagnostic and minor surgical procedures performed on pediatric patients outside of the traditional operating room setting has increased in the past several decades. As a consequence of this change and the increased awareness of the importance of providing analgesia and anxiolysis, the need for sedation for procedures in physicians' offices, dental offices, subspecialty procedure suites, imaging facilities, emergency departments, other inpatient hospital settings, and ambulatory surgery centers also has increased markedly.[1–52] In recognition of this need for both elective and emergency use of sedation in nontraditional settings, the American Academy of Pediatrics (AAP) and the American Academy of Pediatric Dentistry (AAPD) have published a series of guidelines for the monitoring and management of pediatric patients during and after sedation for a procedure.[53–58] The purpose of this updated report is to unify the guidelines for sedation used by medical and dental practitioners; to add clarifications regarding monitoring modalities, particularly regarding continuous expired carbon dioxide measurement; to provide updated information from the medical and dental literature; and to suggest methods for further improvement in safety and outcomes. This document uses the same language to define sedation categories and expected physiologic responses as The Joint Commission, the American Society of Anesthesiologists (ASA), and the AAPD.[56,57,59–61]

This revised statement reflects the current understanding of appropriate monitoring needs of pediatric patients both during and after sedation for a procedure.[3,4,11,18,20,21,23,24,33,39,41,44,47,51,62–73,] The monitoring and care outlined may be exceeded at any time on the basis of the judgment of the responsible practitioner. Although intended to encourage high-quality patient care, adherence to the recommendations in this document cannot guarantee a specific patient outcome. However, structured sedation protocols designed to incorporate these safety principles have been widely implemented and shown to reduce morbidity.[11,23,24,27,30–33,35,39,41,44,47,51,74–84] These practice recommendations are proffered with the awareness that, regardless of the intended level of sedation or route of drug administration, the sedation of a pediatric patient represents a continuum and may result in respiratory depression, laryngospasm, impaired airway patency, apnea, loss of the patient's protective airway reflexes, and cardiovascular instability.[38,43,45,47,48,59,62,63,85–112]

Procedural sedation of pediatric patients has serious associated risks.[2,5,38,43,45,47,48,62,63,71,83,85,88–105,107–138] These adverse responses during and after sedation for a diagnostic or therapeutic procedure may be minimized, but not completely eliminated, by a careful preprocedure review of the patient's underlying medical conditions and consideration of how the sedation process might affect or be affected by these conditions: for example, children with developmental disabilities have been shown to have a threefold increased incidence of desaturation compared with children without developmental disabilities.[74,78,103] Appropriate drug selection for the intended procedure, a clear understanding of the sedating medication's pharmacokinetics and pharmacodynamics and drug interactions, as well as the presence of an individual with the skills needed to rescue a patient from an adverse response are critical.[42,48,62,63,92,97,99,125–127,132,133,139–158] Appropriate physiologic monitoring and continuous observation by personnel not directly involved with the procedure allow for the accurate and rapid diagnosis of complications and initiation of appropriate rescue interventions.[44,63,64,67,68,74,90,96,110,159–174] The work of the Pediatric Sedation Research Consortium has improved the sedation knowledge base, demonstrating the marked safety of sedation by highly motivated and skilled practitioners from a variety of specialties practicing the above modalities and skills that focus on a culture of sedation safety.[45,83,95,128–138] However, these groundbreaking studies also show a low but persistent rate of potential sedation-induced life-threatening events, such as apnea, airway obstruction, laryngospasm, pulmonary aspiration, desaturation, and others, even when the sedation is provided under the direction of a motivated team of specialists.[129] These studies have helped define the skills needed to rescue children experiencing adverse sedation events.

The sedation of children is different from the sedation of adults. Sedation in children is often administered to relieve pain and anxiety as well as to modify behavior (eg, immobility) so as to allow the safe completion of a procedure. A child's ability to control his or her own behavior to cooperate for a procedure depends both on his or her chronologic age and cognitive/emotional development. Many brief procedures, such as suture of a minor laceration, may be accomplished with distraction and guided imagery techniques, along with the use of topical/local anesthetics and minimal sedation, if needed.[175–181] However, longer procedures that require immobility involving children younger than 6 years or those with developmental delay often require an increased depth of sedation to gain control of their behavior.[86,87,103] Children younger than 6 years (particularly those younger than 6 months) may be at greatest risk of an adverse event.[129] Children in this age group are particularly vulnerable

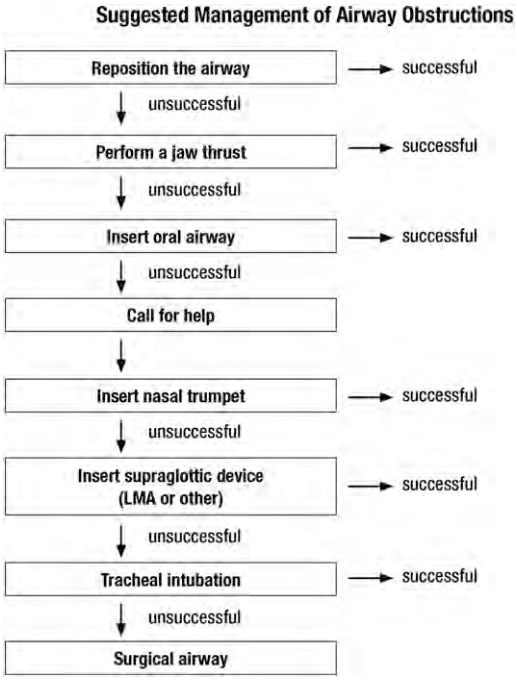

FIGURE 1
Suggested management of airway obstruction.

to the sedating medication's effects on respiratory drive, airway patency, and protective airway reflexes.[62,63] Other modalities, such as careful preparation, parental presence, hypnosis, distraction, topical local anesthetics, electronic devices with age-appropriate games or videos, guided imagery, and the techniques advised by child life specialists, may reduce the need for or the needed depth of pharmacologic sedation.[29,46,49,182–211]

Studies have shown that it is common for children to pass from the intended level of sedation to a deeper, unintended level of sedation,[85,88,212,213] making the concept of rescue essential to safe sedation. Practitioners of sedation must have the skills to rescue the patient from a deeper level than that intended for the procedure. For example, if the intended level of sedation is "minimal," practitioners must be able to rescue from "moderate sedation"; if the intended level of sedation is "moderate," practitioners must have the skills to rescue from "deep sedation"; if the intended level of sedation is "deep," practitioners must have the skills to rescue from a state of "general anesthesia." The ability to rescue means that practitioners must be able to recognize the various levels of sedation and have the skills and age- and size-appropriate equipment necessary to provide appropriate cardiopulmonary support if needed.

These guidelines are intended for all venues in which sedation for a procedure might be performed (hospital, surgical center, freestanding imaging facility, dental facility, or private office). Sedation and anesthesia in a nonhospital environment (eg, private physician's or dental office, freestanding imaging facility) historically have been associated with an increased incidence of "failure to rescue" from adverse events, because these settings may lack immediately available backup. Immediate activation of emergency medical services (EMS) may be required in such settings, but the practitioner is responsible for life-support measures while awaiting EMS arrival.[63,214] Rescue techniques require specific training and skills.[63,74,215,216] The maintenance of the skills needed to rescue a child with apnea, laryngospasm, and/or airway obstruction include the ability to open the airway, suction secretions, provide continuous positive airway pressure (CPAP), perform successful bag-valve-mask ventilation, insert an oral airway, a nasopharyngeal airway, or a laryngeal mask airway (LMA), and, rarely, perform tracheal intubation. These skills are likely best maintained with frequent simulation and team training for the management of rare events.[128,130,217–220] Competency with emergency airway management procedure algorithms is fundamental for safe sedation practice and successful patient rescue (see Figs 1, 2, and 3).[215,216,221–223]

Practitioners should have an in-depth knowledge of the agents they intend to use and their potential complications. A number of reviews and handbooks for sedating pediatric patients are available.[30,39,65,75,171,172,201,224–233] There are specific situations that are beyond the scope of this document. Specifically, guidelines for the delivery of general anesthesia and monitored anesthesia care (sedation or analgesia), outside or within the operating room by anesthesiologists or other practitioners functioning within a department of anesthesiology, are addressed by policies developed by the ASA and by individual departments of anesthesiology.[234] In addition, guidelines for the sedation of patients undergoing mechanical ventilation in a critical care environment or for providing analgesia for patients postoperatively, patients with chronic painful conditions, and patients in hospice care are beyond the scope of this document.

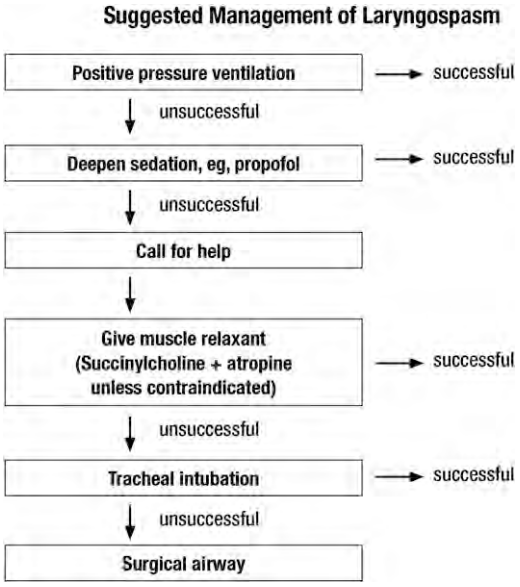

FIGURE 2
Suggested management of laryngospasm.

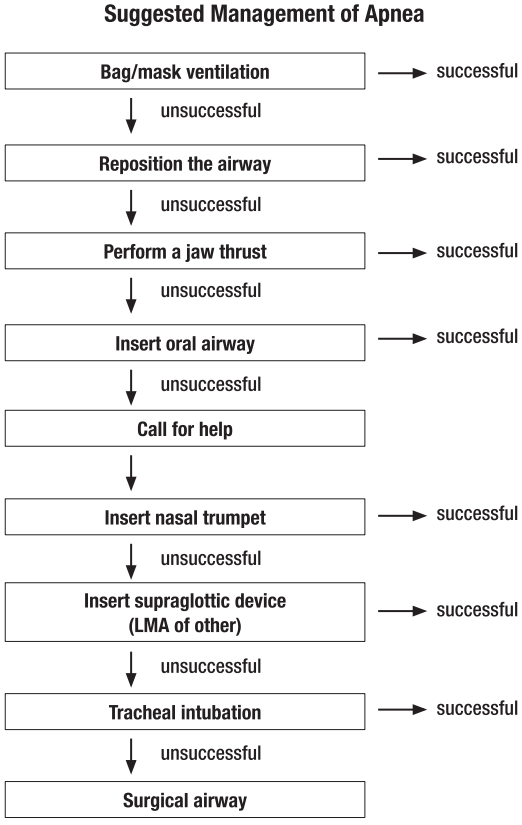

FIGURE 3
Suggested management of apnea.

GOALS OF SEDATION

The goals of sedation in the pediatric patient for diagnostic and therapeutic procedures are as follows: (1) to guard the patient's safety and welfare; (2) to minimize physical discomfort and pain; (3) to control anxiety, minimize psychological trauma, and maximize the potential for amnesia; (4) to modify behavior and/or movement so as to allow the safe completion of the procedure; and (5) to return the patient to a state in which discharge from medical/dental supervision is safe, as determined by recognized criteria (Supplemental Appendix 1).

These goals can best be achieved by selecting the lowest dose of drug with the highest therapeutic index for the procedure. It is beyond the scope of this document to specify which drugs are appropriate for which procedures; however, the selection of the fewest number of drugs and matching drug selection to the type and goals of the procedure are essential for safe practice. For example, analgesic medications, such as opioids or ketamine, are indicated for painful procedures. For nonpainful procedures, such as computed tomography or magnetic resonance imaging (MRI), sedatives/hypnotics are preferred. When both sedation and analgesia are desirable (eg, fracture reduction), either single agents with analgesic/sedative properties or combination regimens are commonly used. Anxiolysis and amnesia are additional goals that should be considered in the selection of agents for particular patients. However, the potential for an adverse outcome may be increased when 2 or more sedating medications are administered.[62,127,136,173,235] Recently, there has been renewed interest in noninvasive routes of medication administration, including intranasal and inhaled routes (eg, nitrous oxide; see below).[236]

Knowledge of each drug's time of onset, peak response, and duration of action is important (eg, the peak electroencephalogram [EEG] effect of intravenous midazolam occurs at ~4.8 minutes, compared with that of diazepam at ~1.6 minutes[237–239]). Titration of drug to effect is an important concept;

one must know whether the previous dose has taken full effect before administering additional drugs.[237] Drugs that have a long duration of action (eg, intramuscular pentobarbital, phenothiazines) have fallen out of favor because of unpredictable responses and prolonged recovery. The use of these drugs requires a longer period of observation even after the child achieves currently used recovery and discharge criteria.[62,238–241] This concept is particularly important for infants and toddlers transported in car safety seats; re-sedation after discharge attributable to residual prolonged drug effects may lead to airway obstruction.[62,63,242] In particular, promethazine (Phenergan; Wyeth Pharmaceuticals, Philadelphia, PA) has a "black box warning" regarding fatal respiratory depression in children younger than 2 years.[243] Although the liquid formulation of chloral hydrate is no longer commercially available, some hospital pharmacies now are compounding their own formulations. Low-dose chloral hydrate (10–25 mg/kg), in combination with other sedating medications, is used commonly in pediatric dental practice.

GENERAL GUIDELINES

Candidates

Patients who are in ASA classes I and II are frequently considered appropriate candidates for minimal, moderate, or deep sedation (Supplemental Appendix 2). Children in ASA classes III and IV, children with special needs, and those with anatomic airway abnormalities or moderate to severe tonsillar hypertrophy present issues that require additional and individual consideration, particularly for moderate and deep sedation.[68,244–249] Practitioners are encouraged to consult with appropriate subspecialists and/or an anesthesiologist for patients at increased risk of experiencing adverse sedation events because of their underlying medical/surgical conditions.

Responsible Person

The pediatric patient shall be accompanied to and from the treatment facility by a parent, legal guardian, or other responsible person. It is preferable to have 2 adults accompany children who are still in car safety seats if transportation to and from a treatment facility is provided by 1 of the adults.[250]

Facilities

The practitioner who uses sedation must have immediately available facilities, personnel, and equipment to manage emergency and rescue situations. The most common serious complications of sedation involve compromise of the airway or depressed respirations resulting in airway obstruction, hypoventilation, laryngospasm, hypoxemia, and apnea. Hypotension and cardiopulmonary arrest may occur, usually from the inadequate recognition and treatment of respiratory compromise.[42,48,92,97,99,125,132,139–155,] Other rare complications also may include seizures, vomiting, and allergic reactions. Facilities providing pediatric sedation should monitor for, and be prepared to treat, such complications.

Back-up Emergency Services

A protocol for immediate access to back-up emergency services shall be clearly outlined. For nonhospital facilities, a protocol for the immediate activation of the EMS system for life-threatening complications must be established and maintained.[44] It should be understood that the availability of EMS does not replace the practitioner's responsibility to provide initial rescue for life-threatening complications.

On-site Monitoring, Rescue Drugs, and Equipment

An emergency cart or kit must be immediately accessible. This cart or kit must contain the necessary age- and size-appropriate equipment (oral and nasal airways, bag-valve-mask device, LMAs or other supraglottic devices, laryngoscope blades, tracheal tubes, face masks, blood pressure cuffs, intravenous catheters, etc) to resuscitate a nonbreathing and unconscious child. The contents of the kit must allow for the provision of continuous life support while the patient is being transported to a medical/dental facility or to another area within the facility. All equipment and drugs must be checked and maintained on a scheduled basis (see Supplemental Appendices 3 and 4 for suggested drugs and emergency life support equipment to consider before the need for rescue occurs). Monitoring devices, such as electrocardiography (ECG) machines, pulse oximeters with size-appropriate probes, end-tidal carbon dioxide monitors, and defibrillators with size-appropriate patches/paddles, must have a safety and function check on a regular basis as required by local or state regulation. The use of emergency checklists is recommended, and these should be immediately available at all sedation locations; they can be obtained from http://www.pedsanesthesia.org/.

Documentation

Documentation prior to sedation shall include, but not be limited to, the following recommendations:

1. Informed consent: The patient record shall document that appropriate informed consent was obtained according to local, state, and institutional requirements.[251,252]
2. Instructions and information provided to the responsible

person: The practitioner shall provide verbal and/or written instructions to the responsible person. Information shall include objectives of the sedation and anticipated changes in behavior during and after sedation.[163,253–255] Special instructions shall be given to the adult responsible for infants and toddlers who will be transported home in a car safety seat regarding the need to carefully observe the child's head position to avoid airway obstruction. Transportation in a car safety seat poses a particular risk for infants who have received medications known to have a long half-life, such as chloral hydrate, intramuscular pentobarbital, or phenothiazine because deaths after procedural sedation have been reported.[62,63,238,242,256,257] Consideration for a longer period of observation shall be given if the responsible person's ability to observe the child is limited (eg, only 1 adult who also has to drive). Another indication for prolonged observation would be a child with an anatomic airway problem, an underlying medical condition such as significant obstructive sleep apnea (OSA), or a former preterm infant younger than 60 weeks' postconceptional age. A 24-hour telephone number for the practitioner or his or her associates shall be provided to all patients and their families. Instructions shall include limitations of activities and appropriate dietary precautions.

Dietary Precautions

Agents used for sedation have the potential to impair protective airway reflexes, particularly during deep sedation. Although a rare occurrence, pulmonary aspiration may occur if the child regurgitates and cannot protect his or her airway.[95,127,258] Therefore, the practitioner should evaluate preceding food and fluid intake before administering sedation. It is likely that the risk of aspiration during procedural sedation differs from that during general anesthesia involving tracheal intubation or other airway manipulations.[259,260] However, the absolute risk of aspiration during elective procedural sedation is not yet known; the reported incidence varies from ~1 in 825 to ~1 in 30 037.[95,127,129,173,244,261] Therefore, standard practice for fasting before elective sedation generally follows the same guidelines as for elective general anesthesia; this requirement is particularly important for solids, because aspiration of clear gastric contents causes less pulmonary injury than aspiration of particulate gastric contents.[262,263]

For emergency procedures in children undergoing general anesthesia, the reported incidence of pulmonary aspiration of gastric contents from 1 institution is ~1 in 373 compared with ~1 in 4544 for elective anesthetics.[262] Because there are few published studies with adequate statistical power to provide guidance to the practitioner regarding the safety or risk of pulmonary aspiration of gastric contents during procedural sedation,[95,127,129,173,244,259–261,264–268] it is unknown whether the risk of aspiration is reduced when airway manipulation is not performed/anticipated (eg, moderate sedation). However, if a deeply sedated child requires intervention for airway obstruction, apnea, or laryngospasm, there is concern that these rescue maneuvers could increase the risk of pulmonary aspiration of gastric contents. For children requiring urgent/emergent sedation who do not meet elective fasting guidelines, the risks of sedation and possible aspiration are as-yet unknown and must be balanced against the benefits of performing the procedure promptly. For example, a prudent practitioner would be unlikely to administer deep sedation to a child with a minor condition who just ate a large meal; conversely, it is not justifiable to withhold sedation/analgesia from the child in significant pain from a displaced fracture who had a small snack a few hours earlier. Several emergency department studies have reported a low to zero incidence of pulmonary aspiration despite variable fasting periods[260,264,268]; however, each of these reports has, for the most part, clearly balanced the urgency of the procedure with the need for and depth of sedation.[268,269] Although emergency medicine studies and practice guidelines generally support a less restrictive approach to fasting for brief urgent/emergent procedures, such as care of wounds, joint dislocation, chest tube placement, etc, in healthy children, further research in many thousands of patients would be desirable to better define the relationships between various fasting intervals and sedation complications.[262–270]

Before Elective Sedation

Children undergoing sedation for elective procedures generally should follow the same fasting guidelines as those for general anesthesia (Table 1).[271] It is permissible for routine necessary medications (eg, antiseizure medications) to be taken with a sip of clear liquid or water on the day of the procedure.

For the Emergency Patient

The practitioner must always balance the possible risks of sedating nonfasted patients with the benefits of and necessity for completing the procedure. In particular, patients with a history of recent oral intake or with other known risk factors, such as trauma, decreased level of consciousness, extreme obesity (BMI ≥95% for age and sex), pregnancy, or bowel motility dysfunction, require careful evaluation before the administration of sedatives. When proper fasting has not been ensured,

the increased risks of sedation must be carefully weighed against its benefits, and the lightest effective sedation should be used. In this circumstance, additional techniques for achieving analgesia and patient cooperation, such as distraction, guided imagery, video games, topical and local anesthetics, hematoma block or nerve blocks, and other techniques advised by child life specialists, are particularly helpful and should be considered.[29,49,182–201, 274,275]

The use of agents with less risk of depressing protective airway reflexes, such as ketamine, or moderate sedation, which would also maintain protective reflexes, may be preferred.[276] Some emergency patients requiring deep sedation (eg, a trauma patient who just ate a full meal or a child with a bowel obstruction) may need to be intubated to protect their airway before they can be sedated.

Use of Immobilization Devices (Protective Stabilization)

Immobilization devices, such as papoose boards, must be applied in such a way as to avoid airway obstruction or chest restriction.[277–281] The child's head position and respiratory excursions should be checked frequently to ensure airway patency. If an immobilization device is used, a hand or foot should be kept exposed, and the child should never be left unattended. If sedating medications are administered in conjunction with an immobilization device, monitoring must be used at a level consistent with the level of sedation achieved.

Documentation at the Time of Sedation

1. Health evaluation: Before sedation, a health evaluation shall be performed by an appropriately licensed practitioner and reviewed by the sedation team at the time of treatment for possible interval changes.[282] The purpose of this evaluation is not only to document baseline status but also to determine whether the patient has specific risk factors that may warrant additional consultation before sedation. This evaluation also facilitates the identification of patients who will require more advanced airway or cardiovascular management skills or alterations in the doses or types of medications used for procedural sedation.

TABLE 1 Appropriate Intake of Food and Liquids Before Elective Sedation

Ingested Material	Minimum Fasting Period, h
Clear liquids: water, fruit juices without pulp, carbonated beverages, clear tea, black coffee	2
Human milk	4
Infant formula	6
Nonhuman milk: because nonhuman milk is similar to solids in gastric emptying time, the amount ingested must be considered when determining an appropriate fasting period.	6
Light meal: a light meal typically consists of toast and clear liquids. Meals that include fried or fatty foods or meat may prolong gastric emptying time. Both the amount and type of foods ingested must be considered when determining an appropriate fasting period.	6

Source: American Society of Anesthesiologists. 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. Available at: https://www.asahq.org/For-Members/Practice-Management/Practice-Parameters.aspx. For emergent sedation, the practitioner must balance the depth of sedation versus the risk of possible aspiration; see also Mace et al[272] and Green et al.[273]

An important concern for the practitioner is the widespread use of medications that may interfere with drug absorption or metabolism and therefore enhance or shorten the effect time of sedating medications. Herbal medicines (eg, St John's wort, ginkgo, ginger, ginseng, garlic) may alter drug pharmacokinetics through inhibition of the cytochrome P450 system, resulting in prolonged drug effect and altered (increased or decreased) blood drug concentrations (midazolam, cyclosporine, tacrolimus).[283–292] Kava may increase the effects of sedatives by potentiating γ-aminobutyric acid inhibitory neurotransmission and may increase acetaminophen-induced liver toxicity.[293–295] Valerian may itself produce sedation that apparently is mediated through the modulation of γ-aminobutyric acid neurotransmission and receptor function.[291,296–299] Drugs such as erythromycin, cimetidine, and others may also inhibit the cytochrome P450 system, resulting in prolonged sedation with midazolam as well as other medications competing for the same enzyme systems.[300–304] Medications used to treat HIV infection, some anticonvulsants, immunosuppressive drugs, and some psychotropic medications (often used to treat children with autism spectrum disorder) may also produce clinically important drug-drug interactions.[305–314] Therefore, a careful drug history is a vital part of the safe sedation of children. The practitioner should consult various sources (a pharmacist, textbooks, online services, or handheld databases) for specific information on drug interactions.[315–319] The US Food and Drug Administration issued a warning in February 2013 regarding the use of codeine for postoperative pain management in children undergoing tonsillectomy, particularly those with OSA. The safety issue is that some children have duplicated cytochromes that allow greater than expected conversion of the prodrug codeine to morphine, thus resulting in potential overdose; codeine should be avoided for postprocedure analgesia.[320–324]

The health evaluation should include the following:

- age and weight (in kg) and gestational age at birth (preterm infants may have associated

sequelae such as apnea of prematurity); and

- health history, including (1) food and medication allergies and previous allergic or adverse drug reactions; (2) medication/drug history, including dosage, time, route, and site of administration for prescription, over-the-counter, herbal, or illicit drugs; (3) relevant diseases, physical abnormalities (including genetic syndromes), neurologic impairments that might increase the potential for airway obstruction, obesity, a history of snoring or OSA,[325–328] or cervical spine instability in Down syndrome, Marfan syndrome, skeletal dysplasia, and other conditions; (4) pregnancy status (as many as 1% of menarchal females presenting for general anesthesia at children's hospitals are pregnant)[329–331] because of concerns for the potential adverse effects of most sedating and anesthetic drugs on the fetus[329,332–338]; (5) history of prematurity (may be associated with subglottic stenosis or propensity to apnea after sedation); (6) history of any seizure disorder; (7) summary of previous relevant hospitalizations; (8) history of sedation or general anesthesia and any complications or unexpected responses; and (9) relevant family history, particularly related to anesthesia (eg, muscular dystrophy, malignant hyperthermia, pseudocholinesterase deficiency).

The review of systems should focus on abnormalities of cardiac, pulmonary, renal, or hepatic function that might alter the child's expected responses to sedating/analgesic medications. A specific query regarding signs and symptoms of sleep-disordered breathing and OSA may be helpful. Children with severe OSA who have experienced repeated episodes of desaturation will likely have altered mu receptors and be analgesic at opioid levels one-third to one-half those of a child without OSA[325–328,339,340]; lower titrated doses of opioids should be used in this population. Such a detailed history will help to determine which patients may benefit from a higher level of care by an appropriately skilled health care provider, such as an anesthesiologist. The health evaluation should also include:

- vital signs, including heart rate, blood pressure, respiratory rate, room air oxygen saturation, and temperature (for some children who are very upset or noncooperative, this may not be possible and a note should be written to document this circumstance);
- physical examination, including a focused evaluation of the airway (tonsillar hypertrophy, abnormal anatomy [eg, mandibular hypoplasia], high Mallampati score [ie, ability to visualize only the hard palate or tip of the uvula]) to determine whether there is an increased risk of airway obstruction[74,341–344];
- physical status evaluation (ASA classification [see Appendix 2]); and
- name, address, and telephone number of the child's home or parent's, or caregiver's cell phone; additional information such as the patient's personal care provider or medical home is also encouraged.

For hospitalized patients, the current hospital record may suffice for adequate documentation of presedation health; however, a note shall be written documenting that the chart was reviewed, positive findings were noted, and a management plan was formulated. If the clinical or emergency condition of the patient precludes acquiring complete information before sedation, this health evaluation should be obtained as soon as feasible.

2. Prescriptions. When prescriptions are used for sedation, a copy of the prescription or a note describing the content of the prescription should be in the patient's chart along with a description of the instructions that were given to the responsible person. **Prescription medications intended to accomplish procedural sedation must not be administered without the safety net of direct supervision by trained medical/dental personnel.** The administration of sedating medications at home poses an unacceptable risk, particularly for infants and preschool-aged children traveling in car safety seats because deaths as a result of this practice have been reported.[63,257]

Documentation During Treatment

The patient's chart shall contain a time-based record that includes the name, route, site, time, dosage/kilogram, and patient effect of administered drugs. Before sedation, a "time out" should be performed to confirm the patient's name, procedure to be performed, and laterality and site of the procedure.[59] During administration, the inspired concentrations of oxygen and inhalation sedation agents and the duration of their administration shall be documented. Before drug administration, special attention must be paid to the calculation of dosage (ie, mg/kg); for obese patients, most drug doses should likely be adjusted lower to ideal body weight rather than actual weight.[345] When a programmable pump is used for the infusion of sedating medications, the dose/kilogram per minute or hour and the child's weight in kilograms should be double-checked and confirmed by a separate individual. The patient's chart shall contain documentation at the time of treatment that the patient's level of consciousness and responsiveness, heart rate, blood pressure, respiratory rate, expired carbon dioxide values, and oxygen saturation

were monitored. Standard vital signs should be further documented at appropriate intervals during recovery until the patient attains predetermined discharge criteria (Appendix 1). A variety of sedation scoring systems are available that may aid this process.[212,238,346–348] Adverse events and their treatment shall be documented.

Documentation After Treatment

A dedicated and properly equipped recovery area is recommended (see Appendices 3 and 4). The time and condition of the child at discharge from the treatment area or facility shall be documented, which should include documentation that the child's level of consciousness and oxygen saturation in room air have returned to a state that is safe for discharge by recognized criteria (see Appendix 1). Patients receiving supplemental oxygen before the procedure should have a similar oxygen need after the procedure. Because some sedation medications are known to have a long half-life and may delay a patient's complete return to baseline or pose the risk of re-sedation[62,104,256,349,350] and because some patients will have complex multiorgan medical conditions, a longer period of observation in a less intense observation area (eg, a step-down observation area) before discharge from medical/dental supervision may be indicated.[239] Several scales to evaluate recovery have been devised and validated.[212,346–348,351,352] A simple evaluation tool may be the ability of the infant or child to remain awake for at least 20 minutes when placed in a quiet environment.[238]

CONTINUOUS QUALITY IMPROVEMENT

The essence of medical error reduction is a careful examination of index events and root-cause analysis of how the event could be avoided in the future.[353–359] Therefore, each facility should maintain records that track all adverse events and significant interventions, such as desaturation; apnea; laryngospasm; need for airway interventions, including the need for placement of supraglottic devices such as an oral airway, nasal trumpet, or LMA; positive-pressure ventilation; prolonged sedation; unanticipated use of reversal agents; unplanned or prolonged hospital admission; sedation failures; inability to complete the procedure; and unsatisfactory sedation, analgesia, or anxiolysis.[360] Such events can then be examined for the assessment of risk reduction and improvement in patient/family satisfaction.

PREPARATION FOR SEDATION PROCEDURES

Part of the safety net of sedation is using a systematic approach so as to not overlook having an important drug, piece of equipment, or monitor immediately available at the time of a developing emergency. To avoid this problem, it is helpful to use an acronym that allows the same setup and checklist for every procedure. A commonly used acronym useful in planning and preparation for a procedure is **SOAPME**, which represents the following:

S = Size-appropriate suction catheters and a functioning suction apparatus (eg, Yankauer-type suction)

O = an adequate Oxygen supply and functioning flow meters or other devices to allow its delivery

A = size-appropriate Airway equipment (eg, bag-valve-mask or equivalent device [functioning]), nasopharyngeal and oropharyngeal airways, LMA, laryngoscope blades (checked and functioning), endotracheal tubes, stylets, face mask

P = Pharmacy: all the basic drugs needed to support life during an emergency, including antagonists as indicated

M = Monitors: functioning pulse oximeter with size-appropriate oximeter probes,[361,362] end-tidal carbon dioxide monitor, and other monitors as appropriate for the procedure (eg, noninvasive blood pressure, ECG, stethoscope)

E = special Equipment or drugs for a particular case (eg, defibrillator)

SPECIFIC GUIDELINES FOR INTENDED LEVEL OF SEDATION

Minimal Sedation

Minimal sedation (old terminology, "anxiolysis") is a drug-induced state during which patients respond normally to verbal commands. Although cognitive function and coordination may be impaired, ventilatory and cardiovascular functions are unaffected. Children who have received minimal sedation generally will not require more than observation and intermittent assessment of their level of sedation. Some children will become moderately sedated despite the intended level of minimal sedation; should this occur, then the guidelines for moderate sedation apply.[85,363]

Moderate Sedation

Moderate sedation (old terminology, "conscious sedation" or "sedation/analgesia") is a drug-induced depression of consciousness during which patients respond purposefully to verbal commands or after light tactile stimulation. No interventions are required to maintain a patent airway, and spontaneous ventilation is adequate. Cardiovascular function is usually maintained. The caveat that loss of consciousness should be unlikely is a particularly important aspect of the definition of moderate sedation; drugs and techniques used should carry a margin of safety wide enough to render unintended loss of consciousness unlikely. Because the patient who

receives moderate sedation may progress into a state of deep sedation and obtundation, the practitioner should be prepared to increase the level of vigilance corresponding to what is necessary for deep sedation.[85]

Personnel

The Practitioner. The practitioner responsible for the treatment of the patient and/or the administration of drugs for sedation must be competent to use such techniques, to provide the level of monitoring described in these guidelines, and to manage complications of these techniques (ie, to be able to rescue the patient). Because the level of intended sedation may be exceeded, the practitioner must be sufficiently skilled to rescue a child with apnea, laryngospasm, and/or airway obstruction, including the ability to open the airway, suction secretions, provide CPAP, and perform successful bag-valve-mask ventilation should the child progress to a level of deep sedation. Training in, and maintenance of, advanced pediatric airway skills is required (eg, pediatric advanced life support [PALS]); regular skills reinforcement with simulation is strongly encouraged.[79,80,128,130,217–220, 364]

Support Personnel. The use of moderate sedation shall include the provision of a person, in addition to the practitioner, whose responsibility is to monitor appropriate physiologic parameters and to assist in any supportive or resuscitation measures, if required. This individual may also be responsible for assisting with interruptible patient-related tasks of short duration, such as holding an instrument or troubleshooting equipment.[60] This individual should be trained in and capable of providing advanced airway skills (eg, PALS). The support person shall have specific assignments in the event of an emergency and current knowledge of the emergency cart inventory. The practitioner and all ancillary personnel should participate in periodic reviews, simulation of rare emergencies, and practice drills of the facility's emergency protocol to ensure proper function of the equipment and coordination of staff roles in such emergencies.[133,365–367] It is recommended that at least 1 practitioner be skilled in obtaining vascular access in children.

Monitoring and Documentation

Baseline. Before the administration of sedative medications, a baseline determination of vital signs shall be documented. For some children who are very upset or uncooperative, this may not be possible, and a note should be written to document this circumstance.

During the Procedure The physician/dentist or his or her designee shall document the name, route, site, time of administration, and dosage of all drugs administered. If sedation is being directed by a physician who is not personally administering the medications, then recommended practice is for the qualified health care provider administering the medication to confirm the dose verbally before administration. There shall be continuous monitoring of oxygen saturation and heart rate; when bidirectional verbal communication between the provider and patient is appropriate and possible (ie, patient is developmentally able and purposefully communicates), monitoring of ventilation by (1) capnography (preferred) or (2) amplified, audible pretracheal stethoscope (eg, Bluetooth technology)[368–371] or precordial stethoscope is strongly recommended. If bidirectional verbal communication is not appropriate or not possible, monitoring of ventilation by capnography (preferred), amplified, audible pretracheal stethoscope, or precordial stethoscope is required. Heart rate, respiratory rate, blood pressure, oxygen saturation, and expired carbon dioxide values should be recorded, at minimum, every 10 minutes in a time-based record. Note that the exact value of expired carbon dioxide is less important than simple assessment of continuous respiratory gas exchange. In some situations in which there is excessive patient agitation or lack of cooperation or during certain procedures such as bronchoscopy, dentistry, or repair of facial lacerations capnography may not be feasible, and this situation should be documented. For uncooperative children, it is often helpful to defer the initiation of capnography until the child becomes sedated. Similarly, the stimulation of blood pressure cuff inflation may cause arousal or agitation; in such cases, blood pressure monitoring may be counterproductive and may be documented at less frequent intervals (eg, 10–15 minutes, assuming the patient remains stable, well oxygenated, and well perfused). Immobilization devices (protective stabilization) should be checked to prevent airway obstruction or chest restriction. If a restraint device is used, a hand or foot should be kept exposed. The child's head position should be continuously assessed to ensure airway patency.

After the Procedure. The child who has received moderate sedation must be observed in a suitably equipped recovery area, which must have a functioning suction apparatus as well as the capacity to deliver >90% oxygen and positive-pressure ventilation (bag-valve mask) with an adequate oxygen capacity as well as age- and size-appropriate rescue equipment and devices. The patient's vital signs should be recorded at specific intervals (eg, every 10–15 minutes). If the patient is not fully alert, oxygen saturation and heart rate monitoring shall be used continuously until appropriate discharge criteria are met (see Appendix 1). Because sedation medications with a long half-life

may delay the patient's complete return to baseline or pose the risk of re-sedation, some patients might benefit from a longer period of less intense observation (eg, a step-down observation area where multiple patients can be observed simultaneously) before discharge from medical/dental supervision (see section entitled "Documentation Before Sedation" above).[62,256,349,350] A simple evaluation tool may be the ability of the infant or child to remain awake for at least 20 minutes when placed in a quiet environment.[238] Patients who have received reversal agents, such as flumazenil or naloxone, will require a longer period of observation, because the duration of the drugs administered may exceed the duration of the antagonist, resulting in re-sedation.

Deep Sedation/General Anesthesia

"Deep sedation" ("deep sedation/analgesia") is a drug-induced depression of consciousness during which patients cannot be easily aroused but respond purposefully after repeated verbal or painful stimulation (eg, purposefully pushing away the noxious stimuli). Reflex withdrawal from a painful stimulus is not considered a purposeful response and is more consistent with a state of general anesthesia. The ability to independently maintain ventilatory function may be impaired. Patients may require assistance in maintaining a patent airway, and spontaneous ventilation may be inadequate. Cardiovascular function is usually maintained. A state of deep sedation may be accompanied by partial or complete loss of protective airway reflexes. Patients may pass from a state of deep sedation to the state of general anesthesia. In some situations, such as during MRI, one is not usually able to assess responses to stimulation, because this would defeat the purpose of sedation, and one should assume that such patients are deeply sedated.

"General anesthesia" is a drug-induced loss of consciousness during which patients are not arousable, even by painful stimulation. The ability to independently maintain ventilatory function is often impaired. Patients often require assistance in maintaining a patent airway, and positive-pressure ventilation may be required because of depressed spontaneous ventilation or drug-induced depression of neuromuscular function. Cardiovascular function may be impaired.

Personnel

During deep sedation, there must be 1 person whose only responsibility is to constantly observe the patient's vital signs, airway patency, and adequacy of ventilation and to either administer drugs or direct their administration. This individual must, at a minimum, be trained in PALS and capable of assisting with any emergency event. At least 1 individual must be present who is trained in and capable of providing advanced pediatric life support and who is skilled to rescue a child with apnea, laryngospasm, and/or airway obstruction. Required skills include the ability to open the airway, suction secretions, provide CPAP, insert supraglottic devices (oral airway, nasal trumpet, LMA), and perform successful bag-valve-mask ventilation, tracheal intubation, and cardiopulmonary resuscitation.

Equipment

In addition to the equipment needed for moderate sedation, an ECG monitor and a defibrillator for use in pediatric patients should be readily available.

Vascular Access

Patients receiving deep sedation should have an intravenous line placed at the start of the procedure or have a person skilled in establishing vascular access in pediatric patients immediately available.

Monitoring

A competent individual shall observe the patient continuously. Monitoring shall include all parameters described for moderate sedation. Vital signs, including heart rate, respiratory rate, blood pressure, oxygen saturation, and expired carbon dioxide, must be documented at least every 5 minutes in a time-based record. Capnography should be used for almost all deeply sedated children because of the increased risk of airway/ventilation compromise. Capnography may not be feasible if the patient is agitated or uncooperative during the initial phases of sedation or during certain procedures, such as bronchoscopy or repair of facial lacerations, and this circumstance should be documented. For uncooperative children, the capnography monitor may be placed once the child becomes sedated. Note that if supplemental oxygen is administered, the capnograph may underestimate the true expired carbon dioxide value; of more importance than the numeric reading of exhaled carbon dioxide is the assurance of continuous respiratory gas exchange (ie, continuous waveform). Capnography is particularly useful for patients who are difficult to observe (eg, during MRI or in a darkened room).[64,67,72,90,96,110,159–162,164–166,167–170,372–375]

The physician/dentist or his or her designee shall document the name, route, site, time of administration, and dosage of all drugs administered. If sedation is being directed by a physician who is not personally administering the medications, then recommended practice is for the nurse administering the medication to confirm the dose verbally before administration. The inspired

concentrations of inhalation sedation agents and oxygen and the duration of administration shall be documented.

Postsedation Care

The facility and procedures followed for postsedation care shall conform to those described under "moderate sedation." The initial recording of vital signs should be documented at least every 5 minutes. Once the child begins to awaken, the recording intervals may be increased to 10 to 15 minutes. Table 2 summarizes the equipment, personnel, and monitoring requirements for moderate and deep sedation.

TABLE 2 Comparison of Moderate and Deep Sedation Equipment and Personnel Requirements

	Moderate Sedation	Deep Sedation
Personnel	An observer who will monitor the patient but who may also assist with interruptible tasks; should be trained in PALS	An independent observer whose only responsibility is to continuously monitor the patient; trained in PALS
Responsible practitioner	Skilled to rescue a child with apnea, laryngospasm, and/or airway obstruction including the ability to open the airway, suction secretions, provide CPAP, and perform successful bag-valve-mask ventilation; recommended that at least 1 practitioner should be skilled in obtaining vascular access in children; trained in PALS	Skilled to rescue a child with apnea, laryngospasm, and/or airway obstruction, including the ability to open the airway, suction secretions, provide CPAP, perform successful bag-valve-mask ventilation, tracheal intubation, and cardiopulmonary resuscitation; training in PALS is required; at least 1 practitioner skilled in obtaining vascular access in children immediately available
Monitoring	Pulse oximetry ECG recommended Heart rate Blood pressure Respiration Capnography recommended	Pulse oximetry ECG required Heart rate Blood pressure Respiration Capnography required
Other equipment	Suction equipment, adequate oxygen source/supply	Suction equipment, adequate oxygen source/supply, defibrillator required
Documentation	Name, route, site, time of administration, and dosage of all drugs administered Continuous oxygen saturation, heart rate, and ventilation (capnography recommended); parameters recorded every 10 minutes	Name, route, site, time of administration, and dosage of all drugs administered; continuous oxygen saturation, heart rate, and ventilation (capnography required); parameters recorded at least every 5 minutes
Emergency checklists	Recommended	Recommended
Rescue cart properly stocked with rescue drugs and age- and size-appropriate equipment (see Appendices 3 and 4)	Required	Required
Dedicated recovery area with rescue cart properly stocked with rescue drugs and age- and size-appropriate equipment (see Appendices 3 and 4) and dedicated recovery personnel; adequate oxygen supply	Recommended; initial recording of vital signs may be needed at least every 10 minutes until the child begins to awaken, then recording intervals may be increased	Recommended; initial recording of vital signs may be needed for at least 5-minute intervals until the child begins to awaken, then recording intervals may be increased to 10–15 minutes
Discharge criteria	See Appendix 1	See Appendix 1

Special Considerations

Neonates and Former Preterm Infants

Neonates and former preterm infants require specific management, because immaturity of hepatic and renal function may alter the ability to metabolize and excrete sedating medications,[376] resulting in prolonged sedation and the need for extended postsedation monitoring. Former preterm infants have an increased risk of postanesthesia apnea,[377] but it is unclear whether a similar risk is associated with sedation, because this possibility has not been systematically investigated.[378]

Other concerns regarding the effects of anesthetic drugs and sedating medications on the developing brain are beyond the scope of this document. At this point, the research in this area is preliminary and inconclusive at best, but it would seem prudent to avoid unnecessary exposure to sedation if the procedure is unlikely to change medical/dental management (eg, a sedated MRI purely for screening purposes in preterm infants).[379–382]

Local Anesthetic Agents

All local anesthetic agents are cardiac depressants and may cause central nervous system excitation or depression. Particular weight-based attention should be paid to cumulative dosage in all children.[118,120,125,383–386] To ensure that the patient will not receive an excessive dose, the maximum allowable safe dosage (eg, mg/kg) should be calculated before administration. There may be enhanced sedative effects when the highest recommended doses of local anesthetic drugs are used in combination with other sedatives or opioids (see Tables 3 and 4 for limits and conversion tables of commonly used local anesthetics).[118,125,387–400] In general, when administering local

TABLE 3 Commonly Used Local Anesthetic Agents for Nerve Block or Infiltration: Doses, Duration, and Calculations

Local Anesthetic	Maximum Dose With Epinephrine,[a] mg/kg		Maximum Dose Without Epinephrine, mg/kg		Duration of Action,[b] min
	Medical	Dental	Medical	Dental	
Esters					
Procaine	10.0	6	7	6	60–90
Chloroprocaine	20.0	12	15	12	30–60
Tetracaine	1.5	1	1	1	180–600
Amides					
Lidocaine	7.0	4.4	4	4.4	90–200
Mepivacaine	7.0	4.4	5	4.4	120–240
Bupivacaine	3.0	1.3	2.5	1.3	180–600
Levobupivacaine[c]	3.0	2	2	2	180–600
Ropivacaine	3.0	2	2	2	180–600
Articaine[d]	—	7	—	7	60–230

Maximum recommended doses and durations of action are shown. Note that lower doses should be used in very vascular areas.

[a] These are maximum doses of local anesthetics combined with epinephrine; lower doses are recommended when used without epinephrine. Doses of amides should be decreased by 30% in infants younger than 6 mo. When lidocaine is being administered intravascularly (eg, during intravenous regional anesthesia), the dose should be decreased to 3 to 5 mg/kg; long-acting local anesthetic agents should not be used for intravenous regional anesthesia.

[b] Duration of action is dependent on concentration, total dose, and site of administration; use of epinephrine; and the patient's age.

[c] Levobupivacaine is not available in the United States.

[d] Use in pediatric patients under 4 years of age is not recommended.

TABLE 4 Local Anesthetic Conversion Chart

Concentration, %	mg/mL
4.0	40
3.0	30
2.5	25
2.0	20
1.0	10
0.5	5
0.25	2.5
0.125	1.25

TABLE 5 Treatment of Local Anesthetic Toxicity

1. Get help. Ventilate with 100% oxygen. Alert nearest facility with cardiopulmonary bypass capability.
2. Resuscitation: airway/ventilatory support, chest compressions, etc. Avoid vasopressin, calcium channel blockers, β-blockers, or additional local anesthetic. Reduce epinephrine dosages. Prolonged effort may be required.
3. Seizure management: benzodiazepines preferred (eg, intravenous midazolam 0.1–0.2 mg/kg); avoid propofol if cardiovascular instability.
4. Administer 1.5 mL/kg 20% lipid emulsion over ∼1 minute to trap unbound amide local anesthetics. Repeat bolus once or twice for persistent cardiovascular collapse.
5. Initiate 20% lipid infusion (0.25 mL/kg per minute) until circulation is restored; double the infusion rate if blood pressure remains low. Continue infusion for at least 10 minutes after attaining circulatory stability. Recommended upper limit of ∼10 mL/kg.
6. A fluid bolus of 10–20 mL/kg balanced salt solution and an infusion of phenylephrine (0.1 μg/kg per minute to start) may be needed to correct peripheral vasodilation.

Source: https://www.asra.com/advisory-guidelines/article/3/checklist-for-treatment-of-local-anesthetic-systemic-toxicity.

anesthetic drugs, the practitioner should aspirate frequently to minimize the likelihood that the needle is in a blood vessel; lower doses should be used when injecting into vascular tissues.[401] If high doses or injection of amide local anesthetics (bupivacaine and ropivacaine) into vascular tissues is anticipated, then the immediate availability of a 20% lipid emulsion for the treatment of local anesthetic toxicity is recommended (Tables 3 and 5).[402–409] Topical local anesthetics are commonly used and encouraged, but the practitioner should avoid applying excessive doses to mucosal surfaces where systemic uptake and possible toxicity (seizures, methemoglobinemia) could result and to remain within the manufacturer's recommendations regarding allowable surface area application.[410–415]

Pulse Oximetry

Newer pulse oximeters are less susceptible to motion artifacts and may be more useful than older oximeters that do not contain updated software.[416–420] Oximeters that change tone with changes in hemoglobin saturation provide immediate aural warning to everyone within hearing distance. The oximeter probe must be properly positioned; clip-on devices are easy to displace, which may produce artifactual data (under- or overestimation of oxygen saturation).[361,362]

Capnography

Expired carbon dioxide monitoring is valuable to diagnose the simple presence or absence of respirations, airway obstruction, or respiratory depression, particularly in patients sedated in less-accessible locations, such as in MRI machines or darkened rooms.[64,66,67,72,90,96,110,159–162,164–170,372–375,421–427] In patients receiving supplemental oxygen, capnography facilitates the recognition of apnea or airway obstruction several minutes before the situation would be detected just by pulse oximetry. In this situation, desaturation would be delayed due to increased oxygen reserves; capnography would enable earlier intervention.[161] One study in children sedated in the emergency department found that the use of capnography reduced the incidence of hypoventilation and desaturation

(7% to 1%).[174] The use of expired carbon dioxide monitoring devices is now required for almost all deeply sedated children (with rare exceptions), particularly in situations in which other means of assessing the adequacy of ventilation are limited. Several manufacturers have produced nasal cannulae that allow simultaneous delivery of oxygen and measurement of expired carbon dioxide values.[421,422,427] Although these devices can have a high degree of false-positive alarms, they are also very accurate for the detection of complete airway obstruction or apnea.[164,168,169] Taping the sampling line under the nares under an oxygen face mask or nasal hood will provide similar information. The exact measured value is less important than the simple answer to the question: Is the child exchanging air with each breath?

Processed EEG (Bispectral Index)

Although not new to the anesthesia community, the processed EEG (bispectral index [BIS]) monitor is slowly finding its way into the sedation literature.[428] Several studies have attempted to use BIS monitoring as a means of noninvasively assessing the depth of sedation. This technology was designed to examine EEG signals and, through a variety of algorithms, correlate a number with depth of unconsciousness: that is, the lower the number, the deeper the sedation. Unfortunately, these algorithms are based on adult patients and have not been validated in children of varying ages and varying brain development. Although the readings correspond quite well with the depth of propofol sedation, the numbers may paradoxically go up rather than down with sevoflurane and ketamine because of central excitation despite a state of general anesthesia or deep sedation.[429,430] Opioids and benzodiazepines have minimal and variable effects on the BIS. Dexmedetomidine has minimal effect with EEG patterns, consistent with stage 2 sleep.[431] Several sedation studies have examined the utility of this device and degree of correlation with standard sedation scales.[347,363,432–435] It appears that there is some correlation with BIS values in moderate sedation, but there is not a reliable ability to distinguish between deep sedation and moderate sedation or deep sedation from general anesthesia.[432] Presently, it would appear that BIS monitoring might provide useful information only when used for sedation with propofol[363]; in general, it is still considered a research tool and not recommended for routine use.

Adjuncts to Airway Management and Resuscitation

The vast majority of sedation complications can be managed with simple maneuvers, such as supplemental oxygen, opening the airway, suctioning, placement of an oral or nasopharyngeal airway, and bag-mask-valve ventilation. Rarely, tracheal intubation is required for more prolonged ventilatory support. In addition to standard tracheal intubation techniques, a number of supraglottic devices are available for the management of patients with abnormal airway anatomy or airway obstruction. Examples include the LMA, the cuffed oropharyngeal airway, and a variety of kits to perform an emergency cricothyrotomy.[436,437]

The largest clinical experience in pediatrics is with the LMA, which is available in multiple sizes, including those for late preterm and term neonates. The use of the LMA is now an essential addition to advanced airway training courses, and familiarity with insertion techniques can be life-saving.[438–442] The LMA can also serve as a bridge to secure airway management in children with anatomic airway abnormalities.[443,444] Practitioners are encouraged to gain experience with these techniques as they become incorporated into PALS courses.

Another valuable emergency technique is intraosseous needle placement for vascular access. Intraosseous needles are available in several sizes; insertion can be life-saving when rapid intravenous access is difficult. A relatively new intraosseous device (EZ-IO Vidacare, now part of Teleflex, Research Triangle Park, NC) is similar to a hand-held battery-powered drill. It allows rapid placement with minimal chance of misplacement; it also has a low-profile intravenous adapter.[445–450] Familiarity with the use of these emergency techniques can be gained by keeping current with resuscitation courses, such as PALS and advanced pediatric life support.

Patient Simulators

High-fidelity patient simulators are now available that allow physicians, dentists, and other health care providers to practice managing a variety of programmed adverse events, such as apnea, bronchospasm, and laryngospasm.[133,220,450–452,] The use of such devices is encouraged to better train medical professionals and teams to respond more effectively to rare events.[128,131,451,453–455] One study that simulated the quality of cardiopulmonary resuscitation compared standard management of ventricular fibrillation versus rescue with the EZ-IO for the rapid establishment of intravenous access and placement of an LMA for establishing a patent airway in adults; the use of these devices resulted in more rapid establishment of vascular access and securing of the airway.[456]

Monitoring During MRI

The powerful magnetic field and the generation of radiofrequency emissions necessitate the use of special equipment to provide

continuous patient monitoring throughout the MRI scanning procedure.[457–459] MRI-compatible pulse oximeters and capnographs capable of continuous function during scanning should be used in any sedated or restrained pediatric patient. Thermal injuries can result if appropriate precautions are not taken; the practitioner is cautioned to avoid coiling of all wires (oximeter, ECG) and to place the oximeter probe as far from the magnetic coil as possible to diminish the possibility of injury. ECG monitoring during MRI has been associated with thermal injury; special MRI-compatible ECG pads are essential to allow safe monitoring.[460–463] If sedation is achieved by using an infusion pump, then either an MRI-compatible pump is required or the pump must be situated outside of the room with long infusion tubing so as to maintain infusion accuracy. All equipment must be MRI compatible, including laryngoscope blades and handles, oxygen tanks, and any ancillary equipment. All individuals, including parents, must be screened for ferromagnetic materials, phones, pagers, pens, credit cards, watches, surgical implants, pacemakers, etc, before entry into the MRI suite.

Nitrous Oxide

Inhalation sedation/analgesia equipment that delivers nitrous oxide must have the capacity of delivering 100% and never less than 25% oxygen concentration at a flow rate appropriate to the size of the patient. Equipment that delivers variable ratios of nitrous oxide >50% to oxygen that covers the mouth and nose must be used in conjunction with a calibrated and functional oxygen analyzer. All nitrous oxide-to-oxygen inhalation devices should be calibrated in accordance with appropriate state and local requirements. Consideration should be given to the National Institute of Occupational Safety and Health Standards for the scavenging of waste gases.[464] Newly constructed or reconstructed treatment facilities, especially those with piped-in nitrous oxide and oxygen, must have appropriate state or local inspections to certify proper function of inhalation sedation/analgesia systems before any delivery of patient care.

Nitrous oxide in oxygen, with varying concentrations, has been successfully used for many years to provide analgesia for a variety of painful procedures in children.[14,36,49,98,465–493] The use of nitrous oxide for minimal sedation is defined as the administration of nitrous oxide of ≤50% with the balance as oxygen, without any other sedative, opioid, or other depressant drug before or concurrent with the nitrous oxide to an otherwise healthy patient in ASA class I or II. The patient is able to maintain verbal communication throughout the procedure. It should be noted that although local anesthetics have sedative properties, for purposes of this guideline they are not considered sedatives in this circumstance. If nitrous oxide in oxygen is combined with other sedating medications, such as chloral hydrate, midazolam, or an opioid, or if nitrous oxide is used in concentrations >50%, the likelihood for moderate or deep sedation increases.[107,197,492,494,495] In this situation, the practitioner is advised to institute the guidelines for moderate or deep sedation, as indicated by the patient's response.[496]

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ABBREVIATIONS

AAP: American Academy of Pediatrics
AAPD: American Academy of Pediatric Dentistry
ASA: American Society of Anesthesiologists
BIS: bispectral index
CPAP: continuous positive airway pressure
ECG: electrocardiography
EEG: electroencephalogram/electroencephalography
EMS: emergency medical services
LMA: laryngeal mask airway
MRI: magnetic resonance imaging
OSA: obstructive sleep apnea
PALS: pediatric advanced life support

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