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## Supplemental Information

### Appendix 1. Recommended Discharge Criteria

1. Cardiovascular function and airway patency are satisfactory and stable.
2. The patient is easily arousable, and protective reflexes are intact.
3. The patient can talk (if age appropriate).
4. The patient can sit up unaided (if age appropriate).
5. For a very young or handicapped child incapable of the usually expected responses, the premedation level of responsiveness or a level as close as possible to the normal level for that child should be achieved.
6. The state of hydration is adequate.

### Appendix 2. ASA Physical Status Classification

Class I	A normally healthy patient.
Class II	A patient with mild systemic disease (e.g., controlled reactive airway disease).
Class III	A patient with severe systemic disease (e.g., a child who is actively wheezing).
Class IV	A patient with severe systemic disease that is a constant threat to life (e.g., a child with status asthmaticus).
Class V	A moribund patient who is not expected to survive without the operation (e.g., a patient with severe cardiomyopathy requiring heart transplantation).

### Appendix 3. Drugs\* That May Be Needed to Rescue a Sedated Patient<sup>44</sup>

Albuterol for inhalation  
 Ammonia spirits  
 Atropine  
 Diphenhydramine  
 Diazepam  
 Epinephrine (1:1000, 1:10 000)  
 Flumazenil  
 Glucose (25 percent or 50 percent)  
 Lidocaine (cardiac lidocaine, local infiltration)  
 Lorazepam  
 Methylprednisolone  
 Naloxone  
 Oxygen  
 Fosphenytoin  
 Racemic epinephrine  
 Rocuronium  
 Sodium bicarbonate  
 Succinylcholine

\* The choice of emergency drugs may vary according to individual or procedural needs.

### Appendix 4. Emergency Equipment<sup>†</sup> That May Be Needed to Rescue a Sedated Patient<sup>‡</sup>

#### Intravenous Equipment

Assorted IV catheters (e.g., 24-, 22-, 20-, 18-, 16-gauge)  
 Tourniquets  
 Alcohol wipes  
 Adhesive tape  
 Assorted syringes (e.g., 1-, 3-, 5-, 10-mL)  
 IV tubing  
     Pediatric drip (60 drops/mL)  
     Pediatric burette  
     Adult drip (10 drops/mL)  
     Extension tubing  
     3-way stopcocks  
 IV fluid  
     Lactated Ringer solution  
     Normal saline solution  
     D<sub>5</sub> 0.25 normal saline solution  
 Pediatric IV boards  
 Assorted IV needles (e.g., 25-, 22-, 20-, and 18-gauge)  
 Intraosseous bone marrow needle  
 Sterile gauze pads

#### Airway Management Equipment

Face masks (infant, child, small adult, medium adult, large adult)  
 Breathing bag and valve set  
 Oropharyngeal airways (infant, child, small adult, medium adult, large adult)  
 Nasopharyngeal airways (small, medium, large)  
 Laryngeal mask airways (1, 1.5, 2, 2.5, 3, 4, and 5)  
 Laryngoscope handles (with extra batteries)  
 Laryngoscope blades (with extra light bulbs)  
     Straight (Miller) No. 1, 2, and 3  
     Curved (Macintosh) No. 2 and 3  
 Endotracheal tubes (2.5, 3.0, 3.5, 4.0, 4.5, 5.0, 5.5, and 6.0 uncuffed and 6.0, 7.0, and 8.0 cuffed)  
 Stylettes (appropriate sizes for endotracheal tubes)  
 Surgical lubricant  
 Suction catheters (appropriate sizes for endotracheal tubes)  
 Yankauer-type suction  
 Nasogastric tubes  
 Nebulizer with medication kits  
 Gloves (sterile and nonsterile, latex free)

† The choice of emergency equipment may vary according to individual or procedural needs.

‡ The practitioner is referred to the SOAPME acronym described in the text in preparation for sedating a child for a procedure.



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

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**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 per-

manent 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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ABBREVIATIONS. AAP, American Academy of Pediatrics; FDA, Food and Drug Administration; USP, US Pharmacopeia; 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,<sup>1</sup> 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.<sup>2,3</sup> Revision of these guidelines placed an emphasis on monitoring, including the routine use of pulse oxime-



try.<sup>4,5</sup> Despite these and other guidelines,<sup>6-10</sup> 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.<sup>11-14</sup> A number of specialties have developed monitoring guidelines that differ from those of the AAP.<sup>5,7,10</sup>

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.<sup>15-27</sup> 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.<sup>28</sup> Investigators of anesthesiology-related mishaps have used critical incident analysis, a tool first developed by the aviation industry, to identify areas of concern.<sup>21,29-38</sup> 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.<sup>15-27,39</sup> Documented problems include: inadequate medical evaluation,<sup>32,40</sup> inadequate monitoring during or after the procedure,<sup>41</sup> inadequate skills in problem recognition and timely intervention,<sup>32</sup> and the lack of experience with a particular age patient or with an underlying medical condition.<sup>32</sup> The importance of an appropriately staffed and equipped recovery facility has also been documented.<sup>42-45</sup> 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.<sup>15,34,46-53</sup>

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.<sup>32</sup> We believed it important to have consensus agreement be-

tween 3 pediatric subspecialties (anesthesiology, critical care, and emergency medicine) so as to minimize bias related to reviewer practice.<sup>36</sup> 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  $\leq 20$  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,  $\chi^2$  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).<sup>54-58</sup> 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. ( <i>Physicians Desk Reference, United States Pharmacopoeia Drug Index, Children's Hospitals Formulary Handbook</i> )	"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 The mother gave two prescriptions of chloral hydrate at home
Prescription given by parent in unsupervised medical environment	"A 22.7 kg child received 432 mg of mepivacaine for a dental procedure. Seizures were followed by respiratory and cardiac arrests"
Local anesthetic overdose—if child received more than the recommended upper limits or if an intravascular injection occurred	"The child received a bottle of milk prior to a CAT scan"
Inadequate fasting for elective procedure	The drug was administered by a technician, there was no physician or nurse in attendance
Unsupervised administration of a drug by a technician	The reviewer could not determine a likely cause of the event
Unknown	

utory causes (Table 1) and these were ranked in order of importance.<sup>59,60</sup> 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 agree-

ment was not by chance alone; there were also moderate  $\kappa$  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 ( $\pm$ standard deviation [SD]) for the entire cohort was  $5.7 \pm 5.5$  years (range, 1 month to 20 years) (Fig 1) and  $21.9 \pm 17.3$  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 ( $6.97 \pm 5.75$  years vs  $3.84 \pm 3.82$  years; mean  $\pm$  SD;  $P = .015$ ), weighed more ( $26.53 \pm 19.85$  kg vs  $16.47 \pm 12.41$  kg; mean  $\pm$  SD;  $P = .021$ ), and were healthier (lower ASA physical status;  $P < .001$ ).

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 ( $\chi^2$ ;  $P = .001$ ) (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

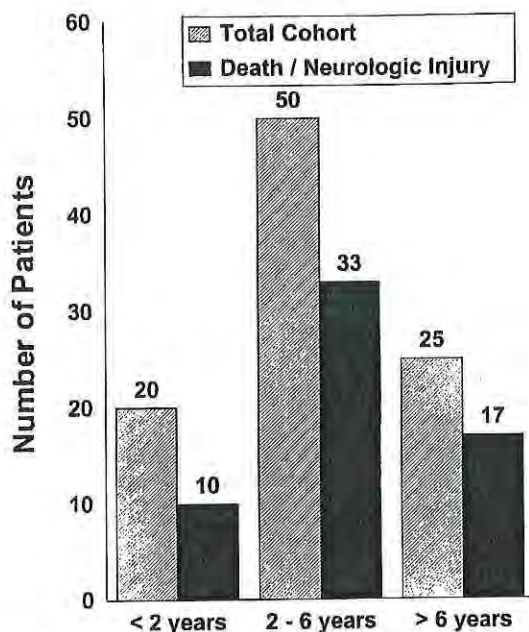


Fig 1. Distribution of cases by age. Note that the majority of patients were 6 years old or less but that there was no relationship between age and adverse outcome.



Airway events = 80% first sign of trouble

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.

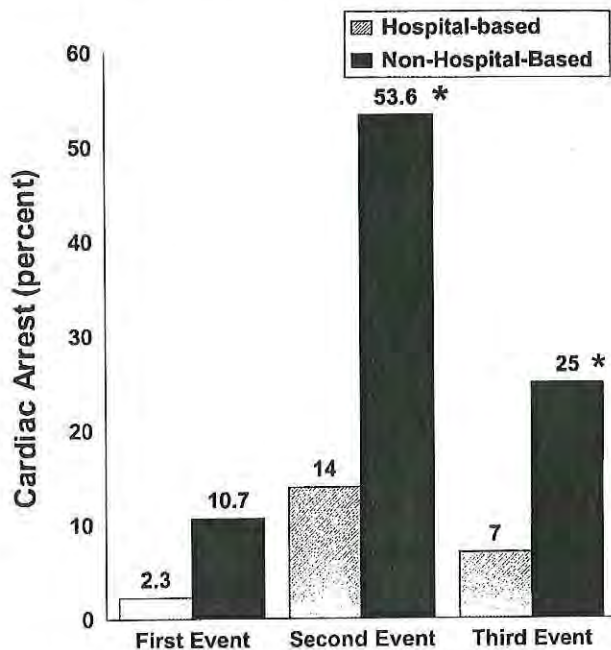


Fig 2. The sequence of presenting medical events revealed that a respiratory event was most common as the presenting event, however, in nonhospital-based facilities the incidence of cardiac arrest as the second or third event was significantly higher ( $*P < .001$ ). These data suggest that either there 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.

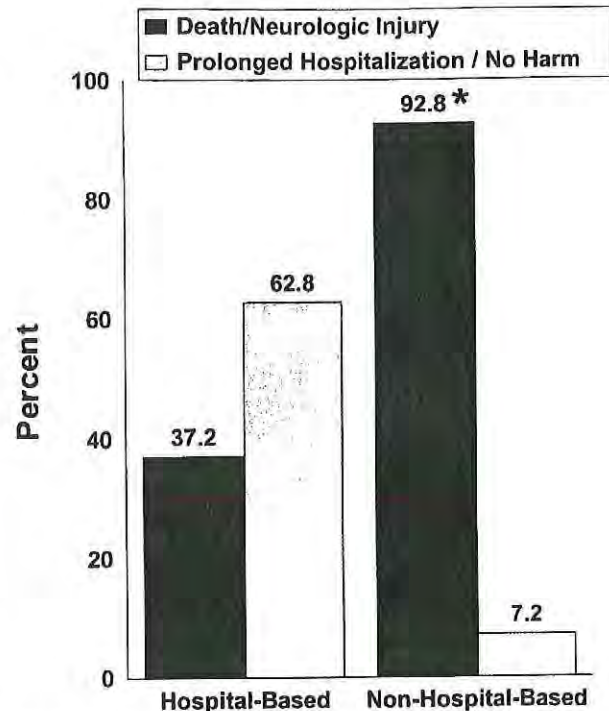


Fig 3. Outcome of adverse sedation-related events in children sedated in hospital-based compared with nonhospital-based facilities. Note that the outcome of death or permanent neurologic injury were significantly greater in nonhospital-based facilities ( $*P < .001$ ).

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.<sup>13,61-65</sup> However, there are important safety concerns regarding the care rendered by a wide variety of prac-

tioners 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.<sup>66</sup> 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.<sup>32,51,67-71</sup> 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.<sup>53</sup> 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.<sup>14,72-74</sup> 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.

Dental

Insurance Coverage

healthy but died



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.<sup>32,67,68</sup> 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.<sup>28,34,46,48,67-69,75</sup> We also recognize that our interpretation of the events may have been influenced in part by knowing the outcome,<sup>36</sup> 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.<sup>4,7-10,76</sup> 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.<sup>21,27,30,34-38,46,48</sup> 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,<sup>21,32,34,52,77</sup> with the aviation industry,<sup>67</sup> and other areas of the transportation industry where human error may have catastrophic consequences.<sup>78,79</sup> 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.<sup>80</sup>

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.<sup>41,81-97</sup> 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.<sup>4,6-10,41</sup> 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.<sup>66</sup> 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.<sup>4,9</sup> 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.<sup>62,97-102</sup>

Rescue Skills



## 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
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: Analysis of Medications Used for Sedation

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**ABSTRACT.** *Objectives.* To perform a systematic investigation of medications associated with adverse sedation events in pediatric patients using critical incident analysis of case reports.

*Methods.* One hundred eighteen case reports from the adverse drug reporting system of the Food and Drug Administration, the US Pharmacopoeia, and the results of a survey of pediatric specialists were used. Outcome measures were death, permanent neurologic injury, prolonged hospitalization without injury, and no harm. The overall results of the critical incident analysis are reported elsewhere. The current investigation specifically examined the relationship between outcome and medications: individual and classes of drugs, routes of administration, drug combinations and interactions, medication errors and overdoses, patterns of drug use, practitioners, and venues of sedation.

*Results.* Ninety-five incidents fulfilled study criteria and all 4 reviewers agreed on causation; 60 resulted in death or permanent neurologic injury. Review of adverse sedation events indicated that there was no relationship between outcome and drug class (opioids; benzodiazepines; barbiturates; sedatives; antihistamines; and local, intravenous, or inhalation anesthetics) or route of administration (oral, rectal, nasal, intramuscular, intravenous, local infiltration, and inhalation). Negative outcomes (death and permanent neurologic injury) were often associated with drug overdose ( $n = 28$ ). Some drug overdoses were attributable to prescription/transcription errors, although none of 39 overdoses in 34 patients seemed to be a decimal point error. Negative outcomes were also associated with drug combinations and interactions. The use of 3 or more sedating medications compared with 1 or 2 medications was strongly associated with adverse outcomes (18/20 vs 7/70). Nitrous oxide in combination with any other class of sedating medication was frequently associated with adverse outcomes (9/10). **Dental special-**

**ists had the greatest frequency of negative outcomes associated with the use of 3 or more sedating medications.** Adverse events occurred despite drugs being administered within acceptable dosing limits. Negative outcomes were also associated with drugs administered by nonmedically trained personnel and drugs administered at home. Some injuries occurred on the way to a facility after administration of sedatives at home; some took place in automobiles or at home after discharge from medical supervision. Deaths and injuries after discharge from medical supervision were associated with the use of medications with long half-lives (chloral hydrate, pentobarbital, promazine, promethazine, and chlorpromazine).

*Conclusions.* Adverse sedation events were frequently associated with drug overdoses and drug interactions, particularly when 3 or more drugs were used. Adverse outcome was associated with all routes of drug administration and all classes of medication, even those (such as chloral hydrate) thought to have minimal effect on respiration. Patients receiving medications with long plasma half-lives may benefit from a prolonged period of postsedation observation. Adverse events occurred when sedative medications were administered outside the safety net of medical supervision. Uniform monitoring and training standards should be instituted regardless of the subspecialty or venue of practice. Standards of care, scope of practice, resource management, and reimbursement for sedation should be based on the depth of sedation achieved (ie, the degree of vigilance and resuscitation skills required) rather than on the drug class, route of drug administration, practitioner, or venue. *Pediatrics* 2000;106:633-644; *sedation, adverse events, critical incident, medication errors, monitoring, guidelines, procedures, systems errors, drug overdose, drug-drug interactions, critical incident analysis.*

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ABBREVIATIONS. AAP, American Academy of Pediatrics; IV, intravenous; INH, inhalation; NS, not significant; PO, oral; IM, intramuscular; SM, submucosal; PR, rectal; IN, intranasal; SC, subcutaneous; DPT, Demerol, Phenergan, and Thorazine; ASA, American Society of Anesthesiologists; AAPD, American Academy of Pediatric Dentists.

**A**dverse sedation-related events occur in children for a variety of reasons. Using critical incident techniques, we reviewed 118 adverse sedation-related incidents in pediatric patients of which 95 provided sufficient information to examine systems issues that contributed to the adverse outcomes.<sup>1</sup> We found that death and permanent neurologic injury were more likely to occur in children sedated in nonhospital-based venues, compared with hospital-based venues, although these children