SPS
SOCIETY FOR PEDIATRIC SEDATION
SAFE AND SOUND

5th International Multidisciplinary Society for Pediatric Sedation Conference

May 23-25, 2010 • Hyatt Regency Louisville • Louisville, KY

SEDATION PROVIDER COURSE • SUNDAY, MAY 23 • KOSAIR CHILDREN'S HOSPITAL

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NORTON HEALTHCARE

SEDATION PROVIDER COURSE SYLLABUS

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Provider Course Information

Target Audience
The target audience for the Sedation Provider Course includes health care providers who have clinical experience in the area of pediatric sedation and who desire to enhance their knowledge and clinical competency in the field. This group includes physicians, nurses and advance-practice nurses involved in the field of pediatric sedation

Statement of Need
This course is designed to meet the needs of the sedation provider seeking both practical (simulation) training and didactic content focused on patient selection, patient safety, pharmacology and the management of common adverse events. As significant adverse events are rare, this "hands-on" model of training is especially pertinent.

Purpose
Participants will gain clinical skills and a deeper understanding regarding issues related to the assessment of sedation patients, development of a sedation plan, recognition and management of both common and life-threatening adverse events in sedation practice and sedation pharmacology. This course is designed to provide practitioners with the knowledge, competencies and skills that promote safe and effective high-quality procedural sedation to children.

Objective
The goal of the provider course is to provide practitioners with the knowledge, competencies and tools to promote high quality procedural sedation to children. Upon successful completion of this course, the registrant should be able to:

1. Perform a pre-sedation risk assessment;
2. Describe the effects of sedation on airway control and respiratory drive;
3. Explain the principles of and interpret the information from pulse oximetry and capnography;
4. Define, diagnose and treat adverse airway and cardiopulmonary events during sedation;
5. Recognize pharmacologic concerns when using common sedative drugs;
6. Apply core case scenarios related to sedated pediatric patients including all aspects of airway management, ventilation, resource management, and appropriate use of resuscitative measures;
7. Develop a systematic and rational approach to pediatric sedation.

Continuing Education Credits
PHYSICIANS
This CME activity has been planned and implemented in accordance with the Essential Areas and Policies of the Kentucky Medical Association through the joint sponsorship of Norton Healthcare and the Pediatric Sedation Society.

Accreditation: Norton Healthcare is accredited by the Kentucky Medical Association to sponsor continuing medical education for physicians.

Designation Statement
Norton Healthcare designates this educational activity for a maximum of 6.75 *AMA PRA Category 1 Credits™* . Physicians should only claim credit commensurate with the extent of their participation in the activity. Physicians are required to sign in daily.

NURSES
Provider: Kosair Children's Hospital - Expiration Date: 12/31/2011 Kentucky Board of Nursing approval of an individual nursing continuing education program does not constitute endorsement of program content. Nursing participants shall attend the entire session and complete the evaluation form. No partial credit can be given. Each attendee must provide license number or employee ID (for Norton Healthcare employees) at time of registration. Refer to each activity's description below for designation of number of contact hours. For questions related to nursing credit, please contact Debora Williams BSN, RN-BC, Clinical Education at Kosair Children's Hospital at phone: (502) 629-7359, fax: (502) 629-8827 or email: Debbie.williams@norton-healthcare.org. Approved by the Kentucky Board of Nursing (KBN) for: Sunday, May 23, 2010 (Day 1): 4-0008-12-11-326 for 6.75 contact hours.

Syllabus Content Sources:
Dartmouth-Hitchcock Medical Center's Course on Pediatric Sedation
Dartmouth-Hitchcock Medical Center
Lebanon Children's Hospital at Dartmouth
Lebanon, NH

Pediatric Procedural Sedation Education Syllabus
University of Wisconsin School of Medicine and Public Health
American Family Children's Hospital
Madison, WI

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PROVIDER COURSE SUPPORTERS

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Provider Course Program

May 23 • Hyatt Regency Louisville • Louisville, KY

SUNDAY, MAY 23, 2010

7:00 am - 7:30 am	Registration and Continental Breakfast
7:30 am - 7:45 am	Introduction Gregory Hollman, MD
7:45 am - 8:30 am	Pre-Sedation Phase and Assessment Patricia D. Scherrer, MD
8:30 am - 8:45 am	Case Scenarios Session Introduction Aaron Calhoun, MD; Akira Nishisaki, MD
8:45 am - 10:15 am	CASE SCENARIOS SESSION I Apnea/Hypoventilation, Airway Obstruction
10:15 am - 10:30 am	Coffee Break
10:30 am - 12:00 n	CASE SCENARIOS SESSION II Secretions/Aspirations, Hemodynamic Changes
12:00 n - 12:45 pm	Lunch
12:45 pm - 1:45 pm	Sedation Phase John W. Berkenbosch, MD
1:45 pm - 4:45 pm	CORE PATIENT SCENARIOS
4:45 pm - 5:30 pm	Testing

Notes

THE SOCIETY FOR PEDIATRIC SEDATION

SEDATION PROVIDER COURSE

Primary Sources

- ***Dartmouth-Hitchcock Medical Center's Course on Pediatric Sedation***
  Dartmouth-Hitchcock Medical Center
  Lebanon Children's Hospital at Dartmouth
  Lebanon, NH

- ***Pediatric Procedural Sedation Education Syllabus***
  University of Wisconsin School of Medicine and Public Health
  American Family Children's Hospital
  Madison, WI

TABLE OF CONTENTS

- **D. SEDATIVE DRUGS**
  - **1. PRIMARY SEDATIVE – ANXIOLYTIC DRUGS**
    - **BENZODIAZEPINES**
      - **(1) DIAZEPAM, MIDAZOLAM, LORAZEPAM**
      - **(2) MIDAZOLAM**
    - **NITROUS OXIDE**
  - **2. PRIMARY SEDATIVE – HYPNOTIC DRUGS "SLEEPERS"**
    - **CHLORAL HYDRATE**
    - **BARBITURATES**
      - **(1) PENTOBARBITAL**
      - **(2) METHOHEXITAL**
    - **CENTRAL ALPHA-2-ADRENERGIC AGONISTS**
      - **(1) CLONIDINE**
      - **(2) DEXMEDETOMIDINE**
    - **ETOMIDATE**
    - **PROPOFOL**
  - **3. PRIMARY SEDATIVE – ANALGESIC DRUGS**
    - **OPIOIDS**
      - **(1) FENTANYL**
      - **(2) MORPHINE**
    - **KETAMINE**
  - **4. REVERSAL AGENTS**
    - **FLUMAZENIL**
    - **NALOXONE**

- **VI. POST – SEDATION PHASE – RECOVERY AND DISCHARGE**
  - **A. RECOVERY AREA AND EQUIPMENT**
  - **B. DISCHARGE CRITERIA**
  - **C. DISCHARGE DOCUMENTATION**
- **VII. ADVERSE EVENTS AND EMERGENCY STATES DURING SEDATION**
  - **A. AIRWAY (PHARYNGEAL) OBSTRUCTION**
  - **B. LARYNGOSPASM**
  - **C. APNEA – HYPOVENTILATION**
  - **D. ASPIRATION**
  - **E. CARDIOVASCULAR INSTABILITY**

SEDATION PROVIDER COURSE

OVERALL COURSE GOAL:
PROVIDE PRACTITIONERS WITH THE KNOWLEDGE, COMPETENCIES AND SKILLS THAT PROMOTE SAFE AND EFFECTIVE HIGH QUALITY PROCEDURAL SEDATION TO CHILDREN

SPECIFIC COURSE OBJECTIVES: COGNITIVE – PSYCHOMOTOR BASED

AM

Describe the current state of pediatric procedural sedation
Define the different levels of sedation and the monitoring needs
Perform a systematic pre-sedation risk assessment
List the necessary equipment required for sedation
Apply basic pharmacologic principles to optimize procedural sedation
Describe the effects of sedative drugs on upper airway tone and respiratory drive

Recognize the most common adverse events that occur during sedation (PSRC data)
Explain the principles of and interpret the information from pulse oximetry and capnography
Define, diagnose and treat apnea and/or hypoventilation
Define, diagnose and treat upper airway obstruction (pharyngeal obstruction, laryngospasm)
Define, diagnose and treat secretions/aspiration
Define, diagnose and treat hemodynamic instability
Perform basic airway maneuvers and bag-mask ventilation

PM

Categorize the different types of procedures requiring sedation in children
Demonstrate knowledge of the pharmacology and uses of common sedative drugs – chloral hydrate, pentobarbital, opioids, benzodiazepines, ketamine, central α2-agonists, nitrous oxide and propofol
Formulate and justify a systematic approach to safe, effective pediatric procedural sedation
Describe the criteria for post-sedation discharge

Demonstrate a methodical approach to providing sedation for invasive procedures
Display a systematic, tailored approach to children undergoing moderately invasive procedures
Exhibit an organized manner to providing deep sedation to children receiving non-invasive radiology procedures
Demonstrate a systematic approach to a child experiencing inadequate sedation

EVALUATION METHODS
Written examination
Simulation testing of specific diagnoses and technical skills
Testing/Simulation testing stations of specific sedation scenarios

INSTRUCTION METHODS
Lectures – Power Point presentations: 2 main lectures, 3 small group lectures, total time
Small group sessions (lecture + hands on stations)
Skill Simulation Stations + Core Case Simulation Stations, total time

I. OVERVIEW OF PEDIATRIC SEDATION

The field of pediatric sedation has evolved significantly over the past two decades. Recognizing the growing number of pediatric procedures requiring sedation outside of the traditional operating room setting, the American Academy of Pediatrics (AAP) first established sedation guidelines in 1985.[1] These guidelines have since been revised in 1992 and more recently in 2006 as sedation practice has expanded across disciplines and locations.[2,3] In 2002 the American Society of Anesthesiology (ASA) also established sedation guidelines for non-anesthesiologists.[4] In 2007 the Society for Pediatric Sedation was formed with the sole mission of promoting safe, effective and accessible procedural sedation to children across all disciplines.

Pediatric procedural sedation is ubiquitous in any hospital that cares for children and, depending on the institution, may be provided by virtually any subspecialty service. Pediatric sedation practice at any one institution is locally governed and influenced by the standards set by that institution. For the most part the guidelines established by the AAP, the ASA and the Joint Commission on Accreditation of Healthcare Organizations (Joint Commission)[5] serve as the standard for institutional policy development in the area of pediatric procedural sedation.

The new regulations stipulated by Joint Commission for moderate and deep sedation clarify qualified staff, appropriate equipment, performance of a "time out", monitoring requirements, documentation of oxygenation, ventilation and circulation and post procedure assessment and care.[5] In addition qualified personnel must have competency based education and training to: evaluate patients presedation, perform sedation and rescue patients who progress to a deeper than planned level of sedation.[5] "Practitioners intending to induce moderate sedation are competent to manage a compromised airway and inadequate oxygenation and ventilation. Practitioners intending to induce deep sedation are competent to manage an unstable cardiovascular system as well as a compromised airway and inadequate oxygenation and ventilation."

Sedation for diagnostic and painful procedures is a growing and dynamic area of pediatric practice. This course is intended to provide you with the basic information and competencies necessary to provide safe and effective sedation. We have designed the course in four parts: 1) the pre-sedation period including risk assessment and general considerations for sedation, 2) the intra-sedation period including the sedation process, monitoring and drugs used for sedation, 3) the post-sedation time period with emphasis on the recovery phase and discharge criteria and 4) adverse events and emergency situations during sedation with focus on recognition and management.

Before beginning this course the student should recognize that we do not intend to present algorithms or a "cook book" on how to perform sedation for a child. Each sedation should take into account the type of procedure that will be performed (i.e. painful vs. non-painful) and the age, developmental status, and personality type of the child. Thought should always be given to how a procedure could be accomplished without medication through the use of preparation, emotional support and/or distraction techniques.

A. SEDATIVE DRUGS

Sedative drugs are medications that result in central nervous system depression. In general a sedative is defined as a drug that decreases activity, moderates excitement and calms the patient. Use of these drugs may result in loss of protective reflexes, with subsequent respiratory and/or cardiac dysfunction.

Many of the clinical effects of medications administered to achieve sedation are dose-related and must be assessed individually for each child. Sedative drugs may be administered orally, intranasally, rectally, parenterally or by inhalation. Specific types of sedatives can be further defined by their characteristic or predominant clinical effect. Some of the more common definitions of drugs used for sedation include:

- Hypnotic: A hypnotic produces drowsiness and facilitates the onset and maintenance of sleep.
- Analgesic: An analgesic relieves pain by altering perception of nociceptive stimuli.
- Anxiolytic: An anxiolytic relieves apprehension and fear due to an anticipated act or illness.
- Amnesic (antegrade): An amnestic agent affects memory incorporation such that the patient is unable to recall events following delivery of the drug.

B. LEVELS OF SEDATION

The transition from minimal to moderate sedation and from moderate to deep sedation can be difficult to predict and must be anticipated whenever sedation is administered. The definitions of minimal sedation, moderate sedation, deep sedation and general anesthesia are defined below.

Professional organizations have defined sedation in different ways. Across the board all these organizations have defined different "levels" of sedation ranging from minimally impaired consciousness to complete unconsciousness or general anesthesia. Any provider who delivers sedation should recognize that different levels of sedation are possible and they are not specific to a given drug. Any drug (given a large enough dose) will produce obtundation, and likewise even the most powerful anesthetic can produce minimal sedation when given in a very small dose.

Sedation providers should recognize that the definitions of sedation depth are arbitrary and there is no clear demarcation between the different levels. The current recommendations from the Joint Commission state that a provider of sedation should be able to manage or "rescue" a patient from one level of sedation "deeper" than that, which is intended. This is in recognition of the fact that it is impossible to always know the effect that a given dose of a sedation medication will have on an individual patient. It is also recognized that different levels of sedation require different levels of practitioner expertise in airway, respiratory and cardiovascular management. Below are the levels of sedation as defined by the AAP and ASA.[3,4]

- **MINIMAL SEDATION (ANXIOLYSIS)**

A drug-induced state in which patients respond normally to verbal commands. Cognitive function and coordination may be impaired. Protective reflexes are maintained and ventilatory and cardiovascular functions are unaffected.

- **MODERATE SEDATION**

A drug-induced depression of consciousness during which patients respond purposefully to verbal commands, either alone or accompanied by light tactile stimulation. No interventions are required to maintain a patent airway and the patient is able to handle secretions without aspiration. Spontaneous ventilation is adequate, although there may be minimal to mild alterations in ventilatory responsiveness. Cardiovascular function is usually maintained. There is significant loss of orientation to environment, with moderate impairment of gross motor function.

- **DEEP SEDATION**

Deep sedation is a medically controlled state of depressed consciousness or unconsciousness from which the patient is not easily aroused. Patients respond purposefully to painful stimulation. It may be accompanied by a partial or complete loss of protective reflexes, which may include the inability to maintain a patent airway independently and respond purposefully to physical stimulation or verbal command. Patients may require assistance in maintaining a patent airway and spontaneous ventilation may be inadequate. Moderate loss of ventilatory responsiveness may occur. Cardiovascular function is usually maintained.

- **GENERAL ANESTHESIA**

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 as well.

Only anesthesiologists are credentialed to administer and/or supervise planned general anesthesia care. Supervised residents and supervised clinical anesthetists are authorized to administer general anesthesia under the medical direction of an anesthesiologist.

Editorial Comment: Many older texts and some sedation providers still refer to "conscious sedation" when they discuss sedation of children. In fact it is extremely difficult – to impossible – to achieve this level of sedation in children. In fact, most sedation in children is either moderate or (more often) deep sedation. Preparation and qualifications for sedation should be planned with this in mind. The AAP now has issued an official statement discouraging the use of the term "conscious sedation" when referencing sedation in children.

Summary of Levels of Sedation and Clinical Response

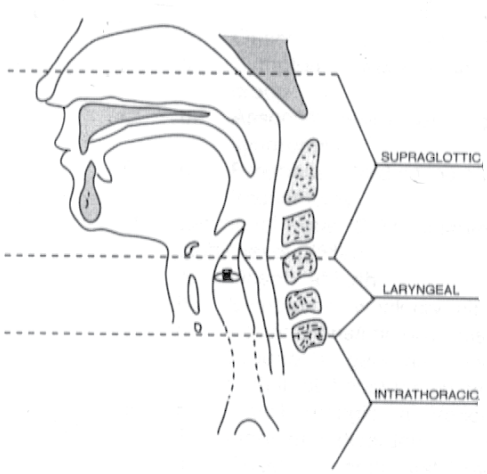
	Verbal Response	**Pain Response**	**Airway Response**	**Breathing**	**Circulation**
Anesthesia Overdose	0	0	0	0	0/+
Anesthesia	0	0	0	0/+	++
Deep Sedation	0	+	+	++	+++
Moderate Sedation	+	++	+++	+++	+++++
Minimal Sedation	+++	++++	++++	+++++	+++++
No Sedation	+++++	+++++	+++++	+++++	+++++

II. SEDATION EFFECTS ON AIRWAY CONTROL AND RESPIRATORY DRIVE

All sedative drugs suppress the central nervous system in a dose-dependent manner. Loss of airway control and respiratory depression are the most common serious adverse effects associated with sedative drug administration. The greater the degree of sedation, the greater the degree of respiratory depression. Respiratory depression increases when combining sedative drugs or when using large doses of a single drug.

A. THE PEDIATRIC AIRWAY

The most important feature of conducting safe pediatric sedation is the ability to assess and manage the pediatric airway. The upper airway is composed of three segments; the supraglottic, laryngeal and intrathoracic.



1. Supraglottic – The supraglottic area consists of the pharyngeal structures and is the most poorly supported and collapsible segment of the upper airway. This segment is the most impacted portion of the airway during sedation.
2. Glottic (larynx) – The glottic structures consist of the vocal cords, subglottic area, and cervical trachea. During sedation the most common cause of airway obstruction in this area is laryngospasm.
3. Intrathoracic – The intrathoracic segment consists of the thoracic trachea and bronchi.

There are a number of developmental characteristics that distinguish the pediatric airway from the adult airway:

- The pediatric airway is smaller in diameter and shorter in length.
- The young child's tongue is relatively larger in the oropharynx.
- The larynx in infants and young children is located more anteriorly.
- The epiglottis in infants and young children is relatively long, floppy, and narrow.
- In children younger than 10 years of age, the narrowest portion of the airway is below the glottis at the level of the cricoid cartilage.

The small caliber of the pediatric upper airway, the relatively large tongue, and the "floppy" and relatively long epiglottis predispose young children to airway obstruction during sedation. In addition, the large occiput of the infant places the head and neck in the flexed position when the patient is placed recumbent, further exacerbating airway obstruction.

During normal inspiration (see figure below), negative intrapleural pressure generated in the thorax creates a pressure gradient from the mouth to the airways, resulting in airflow into the lungs. Extrathoracic airway caliber decreases during inhalation, whereas intrathoracic airway diameter tends to increase. Under normal conditions, changes in airway caliber during respiration are clinically insignificant. Because resistance (R) is inversely proportional to the fourth power of the radius (r^4), narrowing of the pediatric upper airway may increase airway resistance significantly. Elevated airway resistance and the accompanying increased airflow velocity ($\dot{V}$) (Bernoulli effect) require a higher-pressure gradient (ΔP) across the airway if tidal volume and minute ventilation is to be maintained. A greater pressure gradient generated across the airway accentuates the normal inspiratory and expiratory effects on the airway. Consequently, the greater negative pressure generated in the pharynx during inspiration tends to further collapse the upper airway.

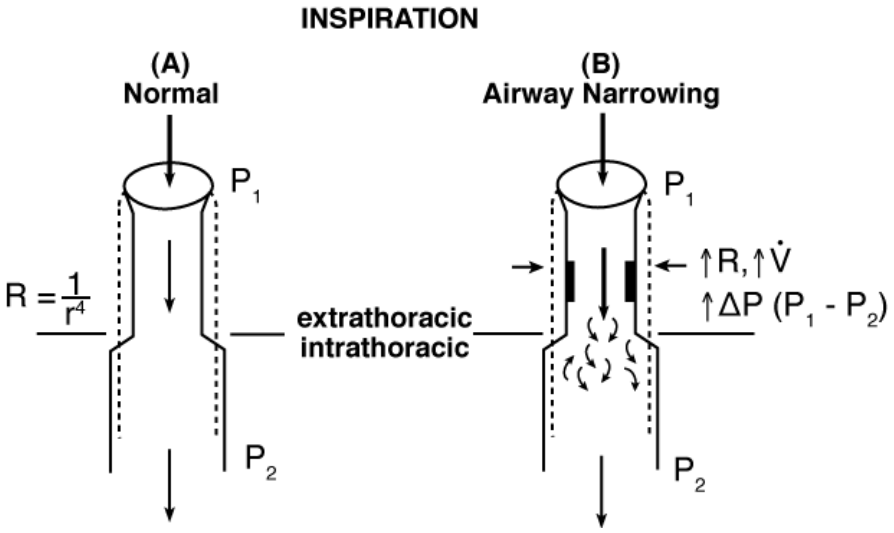


Figure: Changes in airway caliber during inspiration under normal conditions and with airway narrowing.

Airway Control (see figure below)

Pharyngeal Obstruction: Neuromuscular control of the upper airway (CN IX, X and XII) is inhibited to a greater degree than diaphragmatic activity (phrenic nerve) during sedation/anesthesia. The supraglottic area is a collapsible segment located between two relatively well-supported structures, the nasal passage and the trachea. Consequently the negative pressures that develop with diaphragmatic contraction and the reduced overall tone of the upper airway exacerbate the decrease in diameter of the pharynx① during inspiration. During sedation reduced pharyngeal tone results in narrowing of the anterior-posterior distance between the posterior pharynx and the soft palate, epiglottis, and, to a lesser degree, the base of the tongue. As a result the pharyngeal segment functions as a "Starling resistor", a collapsible tube whose caliber is influenced by pressures within the lumen of the airway and soft tissue.[6,7] Airway obstruction during moderate or deep sedation occurs in the supraglottic structures primarily due to the soft palate and epiglottis "falling back" to the posterior pharynx. While it was previously thought that the base of the tongue was the primary cause of upper airway obstruction during unconsciousness, MRI studies of the upper airway in sedated children demonstrate that the soft palate and epiglottis are the most likely structures causing pharyngeal obstruction.[8] Pharyngeal obstruction is the single most common serious adverse event occurring during sedation.

Laryngospasm: The other primary cause of upper airway obstruction during sedation is laryngospasm occurring at the level of the glottis ⬟. Laryngospasm is defined as glottic musculature spasm and may result in partial or complete airway obstruction. Risk factors for laryngospasm include the upper airway secretions, airway manipulation, recent upper respiratory infection, gastroesophageal reflux disease, passive exposure to tobacco smoke, use of an airway device, young age and higher ASA classification.[9] Unlike pharyngeal obstruction simple airway maneuvers do not reverse laryngospasm.

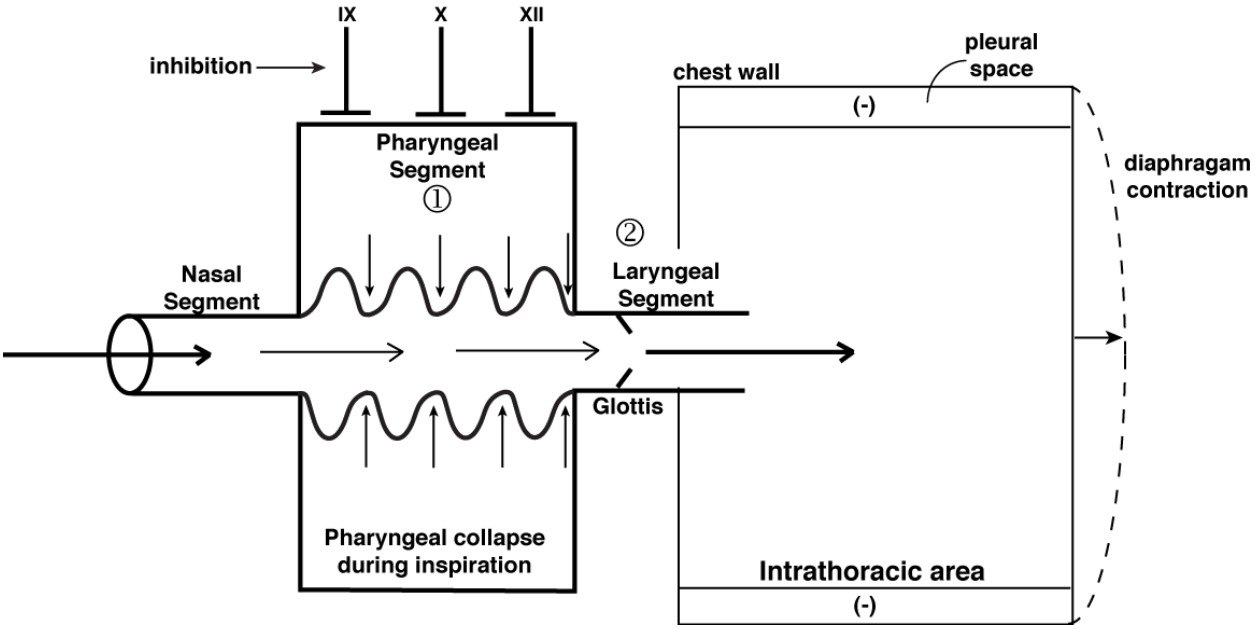


Figure: Segments of the upper airway where obstruction may occur during sedation: ① supraglottic (pharyngeal obstruction) and ⬢ glottic (laryngospasm).

The keys to appropriately managing the pediatric airway during sedation are proper airway positioning and application of positive pressure ventilation when required. Routine management of airway obstruction includes placement of the patient's neck in the sniffing position, often with a rolled towel placed underneath the shoulders and administration of "blow-by" oxygen. If obstruction persists despite these maneuvers, the patient's airway should be repositioned and a chin lift performed to move the supraglottic soft tissue structures, primarily soft palate and epiglottis, anteriorly and away from the posterior pharynx. If a simple chin lift fails to relieve the obstruction, this should be followed by a jaw thrust and application of positive pressure (PEEP) through a flow-inflating anesthesia bag and mask. Supraglottic obstruction and laryngospasm may be difficult to differentiate. One distinguishing feature of complete laryngospasm is the lack of response to simple airway maneuvers. Failure to relieve the obstruction following application of positive pressure suggests complete laryngospasm and requires positive pressure ventilation with cricoid pressure and endotracheal intubation when necessary.

B. RESPIRATORY DRIVE

The basic drive to breath originates from within the central respiratory center located in the brainstem. Output from the respiratory center is modulated by a number of chemical (e.g., CO_2, O_2) and mechanical (e.g. lung mechanics) controllers. Changes in carbon dioxide concentration are among the most important determinants of respiratory drive from the medullary respiratory center. Carbon dioxide freely diffuses across the blood-brain barrier, resulting in an increase in H+ and a decrease in pH in the cerebral spinal fluid. The decrease in pH is accompanied by an increase in neural output from the respiratory center and in minute ventilation. In experimental situations minute ventilation (V_T • RR) typically increases linearly with rises in PCO_2. (See figure below.)

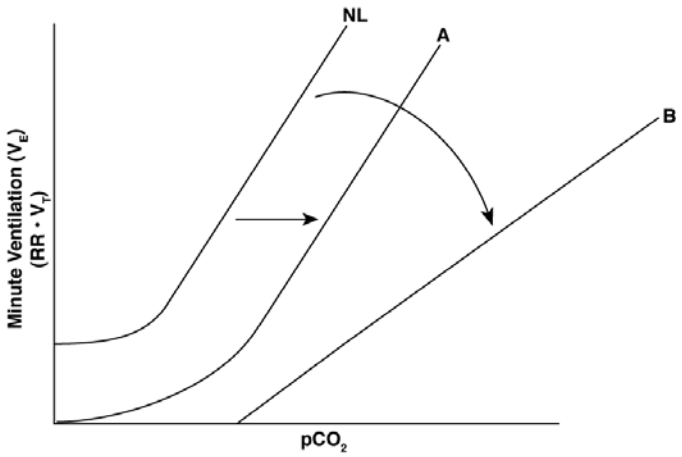


Figure: Minute ventilation response to changing CO_2 concentrations under normal conditions (NL), Minimal Sedation (A) and Deep Sedation (B).

The normal response to increases in carbon dioxide is noted by the line designated NL in the CO_2 ventilation response curve. In general, sedative drugs suppress the central respiratory center and reduce the ventilatory response to a given level of carbon dioxide.[10,11] Doses of sedative drugs that do not cause complete loss of consciousness (e.g., low-dose morphine or midazolam) usually displace only the CO_2 ventilation response curve to the right while maintaining the slope of the response (line A). Under deeper levels of sedation, however, the slope of the CO_2 ventilation response curve decreases as well as shifts to the right (line B).[12] This response may occur when combining sedative drugs or using any sedative that results in unconsciousness. A decreased slope indicates less of an increase in minute ventilation for any given rise in carbon dioxide, a situation that may lead to severe hypercapnia, hypoxemia, or apnea.

III. PROMOTING SAFE AND EFFECTIVE SEDATION

In order to consistently deliver safe and effective sedation, the service delivering sedation must have (1) individuals knowledgeable and competent in providing sedation, (2) an environment with the space and essential resources to provide sedation and (3) a set of policies and procedures that guide the sedation practice. The team, the setting and the structure comprise the foundation of a sedation service.

- **The Team** – The team must be composed of individuals who possess the knowledge and skills to care for patients during all phases of the sedation process. Training must include education in patient assessment, airway management and the pharmacology of sedative drugs and their antagonists.
- **The Setting** – The environment must be conducive to being able to safely and effectively conduct the sedation and procedure. The setting includes the actual sedation facility, monitoring and resuscitative equipment and medications. Ideally the setting is in a family centered environment.
- **The Structure** – The structure includes the program's policies and procedures and defines the "rules" for the sedation practice. Examples include qualified personnel, monitoring requirements, fasting guidelines and recovery and discharge criteria.

The next sections specifically address these key components during the various phases of sedation. The details of these areas will vary from institution to institution (e.g. qualified personnel, training requirements).

IV. PRE-SEDATION PHASE – RISK ASSESSMENT

A presedation assessment is essential to identify high-risk patient populations and anticipate and reduce adverse sedation events. Presedation preparation begins prior to patient arrival. Studies have shown that background knowledge and skills in resuscitation (particularly airway management), education in sedative pharmacology, and presedation risk assessment reduce the frequency and severity of adverse events during sedation. All in all, the majority of preventable adverse sedation events tend to occur as a consequence of inadequate practitioner experience and skills (insufficient education) and violation of hospital policy and procedure (rule violation).[13,14] Several general statements can be made regarding adverse events during sedation:

1. The vast majority of adverse outcomes during sedation are preceded by a respiratory event.
2. The greater the depth of sedation, the greater the risk of complications.
3. The majority of poor outcomes related to adverse sedation events are due to a rule violation or insufficient education and skills of the practitioner.
4. Adverse sedation events are not associated with either a specific sedative drug class or route of administration.

In order to minimize risk (and optimize performance) during procedural sedation, the provider must appreciate all aspects of the sedation encounter associated with the patient, the procedure, and the provider of sedation.

A. FACTORS RELATING TO THE PATIENT

1. GENERAL HISTORY

The general health status of each patient undergoing sedation must be considered. The child must undergo a general physical examination that includes focus on the airway, respiratory and cardiovascular systems. Most institutions require a licensed practitioner prior to sedation complete the physical examination.

For hospitalized patients, the current hospital record may suffice for adequate documentation of presedation health; however, a brief 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, the health evaluation should be obtained as soon as feasible.

In general a relevant presedation history includes the following:

1. Allergies and previous adverse drug reactions
   Adverse Reactions:
   Some patients will have paradoxical reactions to sedative medications such as chloral hydrate where crying and combative behavior is elicited rather than sedation. It is critically important to elicit this information prior to repeating a failed strategy.
   Allergies:
   It is imperative that a good drug allergy history be elicited prior to providing sedation. If a patient states an "allergy" is present to a given medication, a history of what type of reaction occurred should be obtained. Often patients will interpret nausea after sedation as an allergy to whatever medication was given when this is clearly not the case. Drugs, which were associated with urticaria or shortness of breath, are consistent with an allergic reaction and should be avoided.
2. Current medications
3. Sedation/anesthesia history with focus on complications and airway problems
4. History of upper airway problems and sleep disordered breathing or snoring
5. Major medical illnesses, physical abnormalities and neurologic problems.

6. Last oral intake of fluids and solids (see below)
7. Recent acute illnesses (e.g. upper respiratory infection, fever, etc.)
8. Relevant family history (e.g. anesthesia)
9. Review of systems: focus on pulmonary, cardiac, renal and hepatic function

- **FOCUSED REVIEW OF SYSTEMS – "EDCPA"**

Experience (Previous):
When planning to sedate a child, the previous experiences of the patient to be sedated should be elicited. Both good and bad experiences should be reviewed along with the drugs that were previously administered. For example, patients who became combative with a given dose of oral midazolam may not be well served by repeating that drug and dose for another procedure. Similarly the provider should elicit some indication of the anxiety that the patient and family have regarding the upcoming procedure and sedation. The severely anxious patient will often times need significant sedation where a relaxed patient may only need support or distraction. While these facts may seem self evident, a sedation history is often completely neglected by many providers. The response and satisfaction that a patient and family have with a particular sedation will be heavily influenced by their previous experience.

Developmental Issues:
Children younger than one year of age are considered at higher risk than older children.[15] Regardless of age the neurodevelopmental status of the child should be noted. Requirements for sedation will change greatly for any child who is severely delayed. Some of these patients will require more sedation than a similar patient their age while others may actually not require sedation at all. Input from the primary care givers of these patients is critical in determining the amount of intervention that will be required for a given procedure – they can often predict the response a patient will have to a situation – and often it is not what the sedation provider would have guessed after a brief interview and examination. Similarly, input and care from child life personnel may be particularly helpful in calming the patient and subsequently reducing the amount of sedation required. Often these patients have severe scoliosis or limb deformities that require special positioning considerations.

Cardiac:
Most patients with congenital heart disease who are thriving will tolerate sedation without difficulty. However some sedative drugs can significantly affect vascular resistance and may alter pulmonary and systemic blood flow in patients with intra-cardiac shunts. For example, propofol lowers both systemic blood pressure and vascular resistance. In one series, propofol increased right-to-left shunting and decreased PaO_2 values in patients with right-to-left cardiac shunts.[16] While the use of ketamine in patients with pulmonary hypertension remains controversial, a recent report demonstrated no increase in pulmonary pressures following ketamine in children with known pulmonary hypertension receiving sevoflurane anesthesia.[17] Regardless of the sedative agent, however, pulmonary hypertension may be exacerbated if hypoxemia or hypercarbia occur during sedation.

Pulmonary:
Asthma - Respiratory issues usually involve the presence of asthma or upper respiratory tract infections (see below). Although little data exists concerning the risk of sedation for patients with asthma, experts agree that any time there is the chance of manipulating the airway (as is the case with any significant sedation) an asthmatic patient should be in his/her best possible condition prior to beginning the procedure. Generally this includes taking all usual inhalers prior to the sedation and assuring that the child is not actively wheezing. There is no firm data to suggest that giving

prophylactic oral steroids or antihistamines prior to the procedure will change the outcome of a sedated asthmatic child.

Upper Respiratory Tract Infections - Children with upper respiratory tract infections should also be considered separately from those who are well when assessing sedation risk. Unfortunately, during the winter months as many as 20% of the pediatric population may have some symptoms of a respiratory infection. If all these cases were cancelled it would be hard to accomplish a large percentage of our sedation workload. There is little clear data to help categorize the exact increase in risk associated with a current respiratory infection, but several studies have found an increase in airway laryngospasm and respiratory complications after anesthesia is given to patients who have significant cough and mucous production.[18] Prudent practice would dictate that children who have a fever, or those with a significant cough with or without sputum production are best off being postponed for an elective sedation. Likewise, children with wheezing or croup-like symptoms should not be given routine sedation. Children with mild/moderate nasal discharge or those with minimal cough symptoms should be considered for sedation on a case-by-case basis.

Sleep Disordered Breathing – Obstructive Sleep Apnea[19]

Children with sleep-disordered breathing particularly patients with Obstructive Sleep Apnea (OSA) are at significantly greater risk of airway obstruction and oxygen desaturation during sedation.[20] Obesity, adenotonsillar hypertrophy, and upper and lower respiratory problems are among the more common risk factors for OSA.[21,22] In general, patients with OSA should not be moderately or deeply sedated unless airway support is planned.

Aspiration Risk:

A history of last oral intake is required before providing sedation. Although the data on aspiration injury associated with pediatric sedation cases is not definitive, most experts advise fasting guidelines that mimic those required for anesthesia. The reasoning behind these recommendations follows the thought that it is often very difficult to predict the exact depth of sedation that will result from a dose of a sedative in a child – therefore it should be assumed that airway reflexes may be lost and steps to minimize risk should be taken.

There are no national standard guidelines for fasting prior to sedation. Generally accepted guidelines differentiate between clear liquid intake and heavy meals in a graded fashion as outlined below:

Fasting Guidelines:

Food	***Hours of Fasting Required***
Clear Liquids	2
Breast Milk	2 or 4 depending on mother's diet
Formula or Light Meal (no fat)	6
Full Meal	8

In addition to the history of intake, prior to sedation the provider should elicit a history of gastroesophageal reflux disease. Patients who have a history of severe reflux disease (with associated growth failure or daily vomiting) may not be safe under moderate to deep sedation unless their airway is protected. At the very least, these patients should have an assured fasting interval, and some experts will insist on securing their airway with an endotracheal tube prior to providing deep sedation.

With the recommendations outlined above in mind, each provider will need to weigh the urgency of the procedure against the relative risk of the "full stomach". Emergency

departments often do not have the luxury of being able to satisfy fasting guidelines. In such circumstances the benefit/risk ratio of providing sedation must be weighed. Indeed aspiration risk may not be a significant problem in this setting. In spite of this it seems prudent to strive for a reasonable fasting interval when sedating pediatric patients – in particular those having elective procedures.

2. GENERAL PHYSICAL EXAMINATION

As part of the general physical examination baseline vital signs must include blood pressure, heart rate, respiratory rate, and oxygen saturation by pulse oximetry. A physical examination should focus primarily on the upper airway, lungs, cardiovascular system, and baseline neurological status:[23]

1. Upper Airway: assess pharyngeal structures (Mallampati classification), dentition, neck mobility, tonsillar hypertrophy and craniofacial abnormalities.
   - *Habitus:* Receding chin, or significant obesity especially involving the neck and facial structures (body mass index > 35), "unusual facies".

   - *Head and Neck:* Short neck, limited neck extension, decreased hyoid-mental distance (< 3 cm in an adult), neck mass, cervical spine disease or trauma, tracheal deviation, dysmorphic facial features (e.g., Pierre-Robin syndrome), previous tracheostomy, history of head and neck radiation therapy, known or suspected tracheostenosis, or presence of stridor.

   - *Mouth:* Small mouth opening (< 3-cm opening between the upper and lower teeth in an adult); protruding incisors; loose or capped teeth; dental appliances; high, arched palate; macroglossia; nonvisible uvula or tonsillar hypertrophy.

   - *Tonsil Grade*
     0: Tonsils fit within tonsillar fossa
     1+: Tonsils < 25% of space between pillars
     2+: Tonsils < 50% of space between pillars
     3+: Tonsils < 75% of space between pillars
     4+: Tonsils > 75% of space between pillars

     0 1+ 2+ 3+ 4+

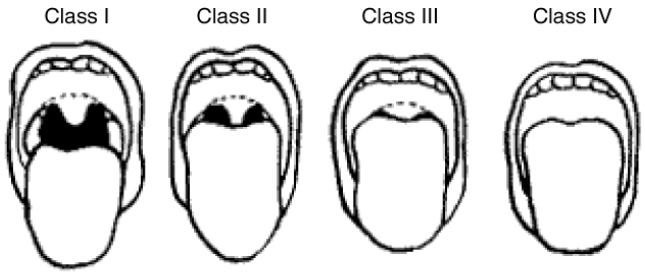
     The incidence of upper airway obstruction during sedation has been demonstrated to increase with enlarged tonsils.[24]

   - *Jaw:* Micrognathia, retrognathia, trismus, or significant malocclusion.

   - *Mallampati classification*[25]*:* It may be helpful to give each child a Mallampati classification as part of the presedation work up. This examination (which classifies the relative size of the tongue in the mouth) may be used as a trigger for referring a patient to an anesthesiologist. In general, a high (III-IV) Mallampati classification associated with any other abnormality of the head and neck is indicative of an airway that may well be difficult to manage.

     To perform the Mallampati examination, the provider has the patient sit facing the examiner and asks the patient to open the mouth as wide as possible. The patient is classified a Mallampati I if the examiner can see down to the tonsillar pillars, class II if the examiner can visualize just the full uvula, class III if only the soft palate

can be seen, and class IV if the hard palate is all that is visualized. Of course many pediatric patients can not cooperate with this examination but any game that encourages a child to open his/her mouth fully should be employed to generally asses the status of the mouth opening and tongue size.



Classification of pharyngeal structures. Note that in Class III the soft palate is visible but in Class IV it is not.

2. Lungs: assess breath sounds, work of breathing and chest wall shape
3. Heart: assess heart tones and peripheral perfusion
4. Neurologic status: determine baseline mental status, ability to control airway, overall muscle tone and signs of focal neurologic problems (e.g. cranial nerve function)

3. AMERICAN SOCIETY OF ANESTHESIOLOGY (ASA) CLASSIFICATION

To aid in assessment of sedation risk, the American Society of Anesthesiology (ASA) has developed a classification system for patients, which categorizes individuals on a general health basis prior to receiving general anesthesia. As such, it is one of the most important factors used to assess the overall presedation risk (see table). Rather than focus on any specific disease entity, the ASA status is intended to group patients together based on health status in order to assess the risk of anesthesia or sedation of a given patient. Several studies have documented the fact that sedation risk in children rises with increasing ASA status.[15,26] ASA 1 and 2 are considered low-risk sedation patient populations. ASA 3 and 4 are high-risk populations.

Table: American Society of Anesthesiology (ASA) Classification

ASA Class	Description	Examples
1	A normal, healthy patient, without organic, physiologic, or psychiatric disturbance	• Healthy with good exercise tolerance
2	A patient with controlled medical conditions without significant systemic effects	• Controlled hypertension • Controlled diabetes mellitus • Controlled seizure disorder • Mild obesity • Age < 1 year • Controlled asthma
3	A patient having medical conditions with significant systemic effects intermittently associated with significant functional compromise	• Poorly controlled hypertension • Moderate obesity • Poorly controlled asthma • Poorly controlled seizures
4	A patient with a medical condition that is poorly controlled, associated with significant dysfunction and is a potential threat to life	• Unstable angina • Symptomatic BPD • Symptomatic heart failure • Acute severe asthma
5	A patient with a critical medical condition that is associated with little chance of survival with or without the surgical procedure	• Multiorgan failure • Sepsis syndrome with hemodynamic instability • Hypothermia • Poorly controlled coagulopathy
6	A patient who is brain dead and undergoing anesthesia care for the purposes of organ donation	
E	This modifier is added to any of the above classes to signify a procedure that is being performed as an emergency and may be associated with a suboptimal opportunity for risk modification	

4. HIGH RISK PATIENT POPULATIONS

Risk categorization is one of, if not the most important aspect of the pre-sedation history and physical exam. In a study of over 7000 children receiving deep sedation with propofol specific patient characteristics were associated with adverse airway events during sedation. Patients with current stridor, snoring, obstructive sleep apnea, morbid obesity, craniofacial malformation, symptomatic asthma or heart disease, gastroesophageal reflex disease, swallowing dysfunction or prior airway problems with sedation or anesthesia experienced oxygen desaturations ~13% of the time compared to 5% in patients without these features.[26] In addition higher risk patients required airway intervention 20% of the time versus 2.6% in lower risk patients.

In addition the University Health System Consortium has identified specific high-risk patient populations in which anesthesia consultation may be warranted.[23]

- Known respiratory compromise/hemodynamic instability
- Obstructive sleep apnea or significant co-morbid conditions
- ASA physical status ≥ 4
- Infants born < 37 weeks EGA who are < 60 weeks post conception
- History of airway compromise during sedation or general anesthesia
- History of adverse reaction to sedation
- Patients with neuromuscular disease affecting respiratory or brain stem function
- High-risk airway by exam

B. FACTORS RELATING TO THE PROCEDURE

***Duration of the procedure**:*
When choosing a sedation medication or technique, the provider should consider the time that the procedure will require to be accomplished. It would seem ill advised to give a sedative medication that lasts for several hours to a child who is having a procedure that only takes several minutes. Likewise the drug given should provide sedation for enough time to accomplish a procedure – or directions for further dosing should be included.

Pain as a side effect of a procedure:
Another important aspect of sedation that must be considered is the presence or absence of pain with a given procedure. Many of the sedatives that are commonly used for sedation – such as chloral hydrate and the benzodiazepines - have absolutely no analgesic component. A child may be sedated with one of these medications but as soon as any painful stimulus is felt, he/she will cry out and thrash about. Adequate movement control is only obtained with non-analgesics (during a painful procedure) when the child has consciousness depressed to deep sedation or general anesthesia levels. Analgesic medications such as fentanyl will provide powerful pain control for procedures while not offering the same sedative potency. In general, analgesic medications should be included if the procedure is going to be painful while they may be omitted for non-painful (diagnostic) procedures.

***Position required for the procedure**:*
In planning the depth of sedation, each provider must consider the position that the patient will be in during the procedure. The average child will maintain an open airway in the supine position even when deeply sedated as long as the neck can be slightly extended. If the head must be flexed during a procedure (e.g. lumbar puncture) or a scan, obstruction of the airway will be much more likely and care should be taken to avoid deep sedation unless the provider is ready to place an oral airway or endotracheal tube. In general when children are placed on their side or in a prone position (e.g. renal biopsy) the airway is at least as easy to maintain – or easier than when in the supine position. Finally if the airway is going to be remote from the sedation provider (i.e. MRI scan) the sedation provider must take into account that adjustment of the airway will not be possible and assisting ventilation will require ceasing the procedure itself.

Anxiety/Stress/Inability to cooperate as a side effect of the procedure:
Sedation may be required for procedures that are not particularly painful and do not require a great deal of movement control but are distressful to the patient. There are several procedures that are particularly emotionally stressful (such as bladder catheterization required for a voiding cystourethrogram) where anxiolysis or even a brief period of unconsciousness will allow the patient to avoid an emotionally harmful experience. Often these procedures involve invasion or examination of the genitalia (sexual abuse evaluations) – and the same amount of discomfort involving an extremity would be trivial. These situations should be considered separately from the seriously painful procedures (bone marrow biopsy) or those where movement control is paramount (MRI scan) yet the need for sedation is no less real.

Availability of Rescue Resources:
The geographical location in which the sedation is taking place will impact the sedation. When sedation is given in a particularly remote area of a medical center or hospital the provider must recognize that “back-up” or “rescue” is going to be much less available. Evaluation of critical incidents related to sedation has revealed that the worst outcomes for unexpected apnea events occur when rescue is not readily available. The depth of sedation provided and the type of patient sedated should be reconsidered when the location of the sedation is more than a 5-minute walk/run from personnel who will be able to help in the case of an emergency.

C. FACTORS RELATING TO THE PROVIDER

Dedicated Sedation Monitor:
The use of moderate or deep sedation shall include 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, as required. It is strongly encouraged that this individual be trained in pediatric basic life support. The support person shall have specific assignments in the event of an emergency and, thus, current knowledge of the emergency cart inventory. The practitioner and all ancillary personnel should participate in periodic reviews of the facility's emergency protocol, to ensure proper function of the equipment and staff interaction.

***Skills Related to Depth of Sedation*:**
Prior to sedating a child or to writing sedation protocols, an honest appraisal of the expertise of the sedation provider must be made. The Joint Commission has recommended that the provider must have the skills necessary to "rescue" a patient from the consequences of sedation one level "deeper" than that, which is intended.[5] Since minimal sedation is often not adequate for an infant or young child undergoing sedation for a procedure, the provider must be able to rescue a child from "deep" sedation or anesthesia. Specifically, if a sedation provider desires moderate sedation for a pediatric patient, he/she should be readily able to perform bag-mask ventilation and ultimately to perform endotracheal intubation. He/she should understand how to quickly and effectively suction the airway and provide intravenous access in an expeditious manner. If these skills are not clearly present for the sedation provider, then minimal sedation should be the goal and sedation protocols should reflect this.

When planning sedation, one must consider the experience and training of the individual who is providing sedation. Many physicians and nurses have the skills outlined above, but have never had experience with sedation medications and have never been trained in how to assess signs of responsiveness and drug titration to effect. Experience in these areas should be sought through practical experience with experts in sedation.

Back-up Systems and Ability to Rescue:
As important as any provider-related issue is the availability of a highly trained and reliable back-up system. Studies of sedation related critical events have shown that sedation accidents are clearly most common in venues where a good back-up or rescue system is not available.[13,27] The depth of sedation that is sought for any procedure should take this factor into account. A protocol for accessing the back-up help for sedation critical events (most often the "code" team) should be clearly laid out and tested on a regular basis. For a nurse who is providing sedation under the direction of a physician, that physician should be present in the area that the sedation is being given and should be available to help out in the case of an emergency.

Table: Summary of Procedure, Patient and Provider Factors

Procedural Factors	Patient Factors	Provider Factors
Pain as a side effect	**Indication** for Procedure	**Skills for depth of sedation** sought
Anxiety/Stress/Inability to Cooperate as a side effect	**ASA Status** (Functional Health)	**Opioid titration skills** for pain management
Expected **Time of Onset** and **Duration**	**Meds/Allergies/Adverse Reactions**	**Sedative hypnotic titration skills** for stress/inability to cooperate management
Required onset **Position**	**Focused ROS-EDCPA:** Previous Experience Developmental Issues Cardiac Pulmonary (asthma, recent URI) Aspiration Risk	**Monitoring skills** for sedation adverse effects
Availability of **Rescue Resources**	**Vitals**-Room air SpO_2	**Skills in mobilizing "rescue' resources**
	Airway Exam	

V. INTRA-SEDATION PHASE

A. GETTING STARTED

1. INFORMED CONSENT, EDUCATION AND "TIME OUT":

Any time sedation medications are to be given to a pediatric patient, a clearly worded informed consent should be obtained from the guardian of the patient. Ideally written informed consent should be obtained although some institutions only require verbal consent. This consent should include a listing of the possible consequences of adverse drug reactions, allergic reactions and airway difficulties. If the patient is old enough to understand the fact that consent is being signed, he/she should be made aware of the document and should be present when the guardian signs the consent. Several institutions now require "assent" from minors prior to beginning sedation for any type of procedure.

Educate the parent (caregiver) and child, if appropriate, prior to administration of the sedative medication regarding the risks and potential adverse effects of sedation, anticipated sedative effects, reason for sedation and potential sedative options. Include information about what the patient can anticipate before, during and after sedation including symptoms and potential side effects. When possible, work out a pre-established signaling system for pain. Where applicable, pre-sedation instruction will be given to the patient (i.e. medication adjustments, NPO requirements, designated driver post procedure, etc.).

"Time Out" refers to the active process of verifying the correct patient, correct procedure, correct site, correct position and correct equipment by those in attendance during the procedure including the patient as appropriate. Prior to the start of the sedated procedure a "Time Out" is to be performed by those in attendance during the procedure. The procedure is not started until any questions or concerns are resolved.

2. EQUIPMENT NEEDS:

Before undertaking sedation of a pediatric patient there are some key pieces of equipment that must be in place – regardless of the desired depth of sedation that is intended. The exact location of the equipment and how "immediately available" each device is for every sedation will vary with the drugs used and the intended level of sedation, but in any case this equipment is crucial to the safe care of a sedated pediatric patient.

Many providers have developed mnemonics in order to remember this equipment and remind themselves of what should be in place prior to starting sedation. One such mnemonic is: SOAPME[3]:

S (suction) – size-appropriate suction catheters and a functioning suction apparatus (e.g., Yankauer-type suction)

O (oxygen) – adequate oxygen supply and functioning flow meters or other devices to allow its delivery

A (airway) – size-appropriate airway equipment: nasopharyngeal and oropharyngeal airways, laryngoscope blades (checked and functioning), endotracheal tubes, stylets, facemask, bag-valve-mask or equivalent device (functioning)

P (pharmacy) – all the resuscitation drugs needed for an emergency, sedatives, and sedative antagonists

M (monitors) – pulse oximeter with size-appropriate probes and other monitors as appropriate for the procedure (e.g., noninvasive blood pressure, end-tidal carbon dioxide, ECG, stethoscope, pre-tracheal stethoscope)

E (extra equipment) – special equipment or drugs for a particular case (e.g., defibrillator)

Sedation providers may also think in terms of categories of equipment that are crucial. The one that might match the categories of equipment in this course is **SOBA MDI** (**S**uction **O**xygen **B**ag-mask **A**irways **M**onitors **D**rugs **I**v-access).

Suction:
A suction apparatus must be available during any pediatric sedation. A portable suction machine must be present during patient transport. Emesis with/without aspiration is clearly a rare event in sedation practice, but when it does occur appropriate suctioning of gastric contents from the airway may make the difference between a minor incident and a major injury. More often suctioning comes in handy as a way to clear the airway of secretions that can inhibit spontaneous ventilation and cause coughing and oxygen desaturation. The best general-purpose option is an appropriately sized Yankhaur suction device that will readily suction food material and secretions from the upper airway. Suction catheters of various sizes may also be helpful, but care must be taken with these devices as deep airway suctioning can stimulate powerful vagal responses as well as laryngospasm when done too vigorously. Nasal suctioning should be done with caution as it can result in significant bleeding from the turbinates.

Oxygen:
Anytime sedation is to be induced in a child, a reliable source of oxygen should be present. This source is typically the "wall" oxygen that is provided in a given institution. In cases where deep sedation or anesthesia is to be induced (and oxygen delivery is critical), a second "back-up" source of oxygen is helpful in case the institutional supply fails. Most often this would take the form of an "E" sized cylinder of oxygen with an oxygen flow meter attached. In cases where wall oxygen is not available, the provider should check the oxygen tank supply and assure that there is ample oxygen available for the case – and/or that there are back-up oxygen tanks available.
Oxygen Delivery: Supplemental oxygen is recommended for any child undergoing deep sedation. Methods of oxygen administration include:

1. Nasal cannula: The nasal cannula provides up to 44% oxygen. It is a low flow system where tidal volume from the patient mixes with room air. The inspired percent oxygen will depend on the flow rate and the patient's tidal volume. The addition of each liter of oxygen flow increases the inspired oxygen percent by approximately 4%. One liter of flow per minute increases FiO_2 from 21% to 24% while six liters per minute will increase the FiO_2 to 44%. The cannula can be secured if necessary with transparent occlusive dressing on each cheek.

2. Simple facemask: The simple facemask provides up to 60% FiO_2. Flow rate is usually set between six to 10 liters per minute. The mask should extend from the bridge of the nose to the cleft of the chin. The correctly sized mask fits tightly without placing excessive pressure on the eyes. Place the mask on the face starting from the nose downward and adjust the nose, cleft and head strap. Liter flow must be six liters per minute or greater to prevent accumulation of carbon dioxide in the mask. A non-rebreather mask at 10-12 liters per minute (or a flow rate to keep the reservoir bag inflated) is indicated in the patients who require high oxygen concentrations and can achieve FiO_2 concentrations of 60-90%.

Bag and Mask:

A bag and mask for positive pressure ventilation must be present for any sedation. This may take the form of an "anesthesia" bag or self-inflating bag. If the anesthesia bag is to be used, the provider must understand how to adjust the flow rates and valves to allow good positive pressure ventilation (PPV). Likewise, the provider should be familiar with the self-inflating bags, which are often supplied with "pop-off" valves, which may need to be closed for positive pressure ventilation. The exact arrangement of the "tail" on this bag that allows for high-inspired fraction of oxygen should also be reviewed.

A variety of different sized masks should be available. They should be constructed in a way that will allow a good seal to be made with the face of the sedated patient - should PPV be required. These masks may be round or triangular in shape. They may have also an inflatable cuff. Bag-mask ventilation should be practiced (and proficiency should be documented) with the type of bag and mask that is available at the site of the sedation prior to having to use this equipment in an emergency. Since PPV is made much easier in infants and children when an appropriate oral airway is in place, a variety of sizes of oral airways should be present to assist with ventilation.

Airways:

Airway equipment is crucial to the safe conduct of pediatric sedation.

Oropharyngeal Airways:

Oropharyngeal airways are S-shaped devices that hold the tongue away from the posterior wall of the pharynx. They are most helpful in the spontaneously breathing patient who is semiconscious and at risk of occluding the airway via tongue and pharyngeal relaxation.

Nasopharyngeal Airways:

Nasopharyngeal airways are uncuffed tubes made of soft rubber or plastic. They are used most frequently for the intoxicated or semiconscious patient who cannot tolerate an oropharyngeal airway. A nasopharyngeal airway is indicated when insertion of an oropharyngeal airway is technically difficult or impossible because of a strong gag reflex, trismus, massive trauma around the mouth, or wiring of the upper and lower jaws.

Laryngoscopes and Endotracheal Tubes:

Even with the most careful titration of sedation medication, the sedation provider must be prepared for the rare instance where a child will become apneic and require prolonged positive pressure ventilation. In these cases definitive airway control with an endotracheal tube may be preferred. Because of this, laryngoscope blades of appropriate size for each patient undergoing sedation must be available in the immediate area of the child undergoing sedation. In general it is easiest to keep a supply of #0-3 Miller blades and 1-3 MacIntosh blades cleaned and ready for use. The batteries for the laryngoscope handles should also be tested at regular intervals. Endotracheal tubes sized to fit each patient should also be handy. Once again it is often easiest to stock a supply of cuffed endotracheal tubes from size 3-7.0 mm and replace each tube as it is used.

Laryngeal Mask Airways (LMA's):

The LMA has become increasingly popular for airway management during anesthesia and in emergency situations. It is quite easy to place after sufficient training. While most sedation providers (non-anesthesiologists) will not be very familiar with their use, having various sizes available (size 1.5 – 4) in case of emergency will aid anyone who is familiar

with their use – particularly in the case of individuals with airways that are difficult to intubate.

Monitoring Devices:
Another key to safe sedation is the use of appropriate monitoring devices. The current AAP guidelines do not specifically require a particular set of monitors. They do state however that "Vital signs, including oxygen saturation and heart rate, must be documented at least every 5 minutes in a time based record."[3] The most commonly used array of monitors for sedation includes pulse oximetry, electrocardiography and noninvasive blood pressure monitoring. Pulse oximetry, capnography, ECG and blood pressure monitoring will be reviewed in the Monitoring section below.

Drugs for Emergency Resuscitation:
Drugs for resuscitation purposes must be readily available. Examples of important resuscitative medications include:

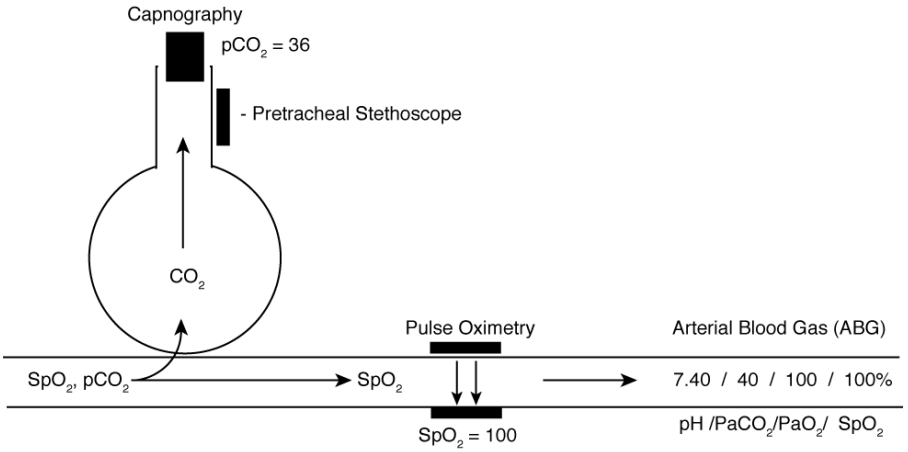
Albuterol (2.5 mg/3 ml)
Atropine (0.4 mg/ml)
Calcium chloride (100 mg/ml)
Dextrose 50% (0.5 g/ml)
Diphenhydramine (50 mg/ml)
Epinephrine 1:1000 (1 mg/ml)
Epinephrine 1:10,000 (0.1 mg/ml)
Flumazenil (0.5 mg/5 ml)
Lidocaine (100 mg/5 ml)
Naloxone (1 mg/ml)
Vecuronium (1 mg/ml)

Intra-vascular Access:
Children undergoing deep sedation should have an intravenous catheter in place. The availability of intravenous access allows the practitioner to administer medications that can immediately treat airway obstruction, reverse bradycardia and administer specific reversal drugs for patients who become oversedated with benzodiazepines and opioids. Intravenous access also provides the practitioner with the ability to titrate sedative medications to a desired clinical effect.

B. MONITORING

Monitoring the effects of sedative drugs is essential to promote the highest level of safety and effectiveness during sedation. Because of the significant effect sedatives have on airway control and respiratory drive, the most important monitoring tools are those that assess breathing. As the depth of sedation increases so does the risk, particularly respiratory. Consequently, assessing the level of consciousness during sedation is a key part of the monitoring process. The following section discusses the monitoring tools commonly used to assess oxygenation and ventilation.

RESPIRATORY MONITORING



1. MONITORING GAS EXCHANGE – GENERAL PRINCIPLES

Monitoring the patient's respiratory status is important to insure patient safety during sedation. Pulse oximetry and capnography are the two primary methods used to assess gas exchange during sedation and serve as practical, noninvasive surrogates to arterial blood gas analysis (ABG). While routine ABG analysis is impractical in most sedated pediatric patients, it remains the gold standard in assessment of gas exchange. Understanding the measurable components of the ABG (pH, $PaCO_2$, PaO_2 and SpO_2) is helpful in accurately interpreting the information received by pulse oximetry and capnography. The normal values of an ABG in room air are: pH: 7.35-7.45, $PaCO_2$: 35-45, PaO_2: 95-100 and SpO_2: 95-100.

- Arterial Carbon Dioxide ($PaCO_2$) and pH – The arterial CO_2 is the primary indicator of the effectiveness of alveolar ventilation ($\dot{V}_A$). $PaCO_2$ values are influenced by two factors, the degree of alveolar ventilation and amount of CO_2 production. $\dot{V}_A$ is equal to the respiratory rate (RR) times the volume of alveolar (V_A) gas exhaled. $PaCO_2$ is inversely proportional to alveolar ventilation and directly proportional to the amount of CO_2 produced by the body ($\dot{V}CO_2$).

  $PaCO_2 = \dot{V}CO_2/\dot{V}_A$

  In the face of a constant $\dot{V}CO_2$ any decline in ventilation ($\dot{V}_A$) will result in a rise of CO_2. Hypercarbia is defined as a carbon dioxide value > 45 mmHg and is indicative of hypoventilation (i.e. low $\dot{V}_A$). Hypoventilation is particularly common during deep sedation and may result from either a reduction in tidal volume, respiratory rate or both. Acute changes in $PaCO_2$ result in predictable changes in pH. When pCO_2 increases ~ 20 mm Hg, pH falls by ~ 0.1. A typical pH and pCO_2 during deep sedation would be 7.35 (pH) and 50 (pCO_2).

- Arterial pO_2 (PaO_2) and Oxygen Saturation (SpO_2) - Under normal circumstances the partial pressure of oxygen (PaO_2) determines the degree of oxygen saturation as defined by the Hemoglobin-Oxygen dissociation curve (see figure below). Normal values of PaO_2 (~95-100 mmHg) result in SpO_2 values of 96 to 100% Ⓐ. PaO_2 values of 60 mmHg Ⓑ (hypoxemia) correspond to SpO_2 values of approximately 88-92%. In the absence of lung disease, hypoventilation alone can result in low PaO_2 and SpO_2 values based on the alveolar gas equation. For example in room air when pCO_2 rises to approximately 60 mmHg, PaO_2 values fall to ~ 70-75 mmHg Ⓒ. By supplementing oxygen ($\uparrow FiO_2$), PaO_2 values can rise to levels that bring SpO_2 to normal values, "masking" signs of hypercarbia.

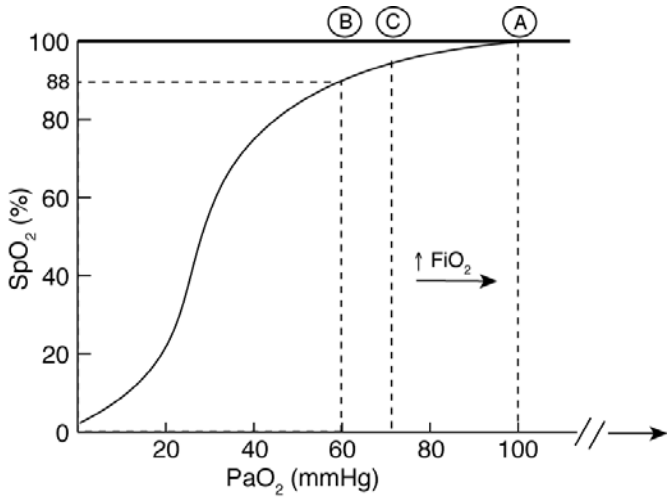
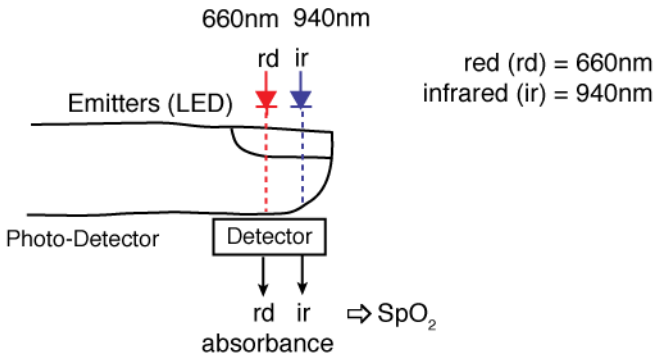


Figure: Hemoglobin – Oxygen Dissociation Curve - Ⓐ Normal PaO_2 values, Ⓑ PaO_2 of 60 mmHg and corresponding SpO_2 values ~88% and Ⓒ PaO_2 of ~75 mmHg in room air as a consequence of hypoventilation (pCO_2=60), ↑ FiO_2 raises PaO_2 back to normal values.

2. MONITORING OXYGENATION

PULSE OXIMETRY[28]

Pulse oximetry is an important noninvasive monitoring technique that allows continuous evaluation of arterial oxygen saturation in the sedated pediatric patient. The two basic requirements of commercially available pulse oximeters are the presence of a pulsatile tissue bed (arterial vessel) and the spectrophotometric analysis of oxygenated hemoglobin and nonoxygenated hemoglobin. The absorption spectra of oxygenated hemoglobin peaks at 940 nm (infrared light) whereas deoxygenated hemoglobin peaks at 660 nm (red light). The spectrophotometric method is based on the amount of light absorbed from two light emitting diodes (LEDs) across the tissue bed. A microprocessor in the pulse oximeter determines the relative proportions of red and infrared light to calculate the percentage of oxygenated versus nonoxygenated hemoglobin in the tissue bed.



Pulse oximetry must be applied to all children undergoing moderate to deep sedation.[3] The determination of oxygen saturation in patients undergoing sedation is used to identify problems with oxygenation and to regulate oxygen therapy. Note that pulse oximeters assess oxygenation and do not evaluate carbon dioxide elimination. It is important for patients to have hemoglobin oxygen saturation above 90%. Oxygen saturations ≤90% are generally considered clinically significant, and in the sedated patient without underlying lung disease indicate significant hypoventilation. A characteristic arterial blood gas in the

presence of hypoventilation and no supplemental oxygen reveals hypoxemia and hypercarbia. Since pulse oximetry requires pulsatile blood flow to determine oxygen saturation, pulse oximeters vary in accuracy and strength signal in the presence of poorly perfused tissues. Low or absent pulse signals will occur under these circumstances. Similarly, when the patient is actively moving, the pulse oximeter may have difficulty distinguishing pulsatile tissue beds from movement-induced artifact. The latest versions of these monitors have software and largely eliminate the motion and light interference that plagued earlier versions. There is typically a time delay of at least 15 to 20 seconds between change in oxygen saturation and its detection by a pulse oximeter. Thus, evidence of oxygen desaturation by pulse oximetry gives a comparatively late warning of hypoxia. Placement of the pulse oximeter probe in a more central location (e.g. ear) may reduce the delay in the determination of oxygen desaturation. Finally, pulse oximetry does not provide direct information regarding ventilation. Consequently CO_2 and pH are not assessed with pulse oximetry.

Anything that obstructs arterial blood flow may disrupt sensing by the pulse oximeter. This technology will also not work when compounds such as dyes or unusual forms of hemoglobin confuse the calculation mentioned above. In general pulse oximeters are very accurate (within ~1-2%) and give two crucial pieces of information for any child under sedation– oxygen saturation of the hemoglobin and pulse rate.

Pulse Oximeter Sensor Selection

- Chose appropriate size and type of sensor.
  - Reusable sensors are for spot checks or short-term use
  - Disposable adhesive sensors are for continuous monitoring
- Place sensor so that the light beams and photo sensor are opposite each other.
- Warm cold extremities to improve circulation.
- Avoid extremity with blood pressure cuff, arterial line or tourniquet.
- Avoid placing sensor on an area that is moved frequently.
- Remove nail polish or dirt, which may not allow light beams to pass through the tissue.
- Clean dirt off reusable sensor.
- Protect sensor from bright external light sources by covering the sensor and the limb it is on.

Trouble Shooting when Pulse Oximeter Readings are Low

- Assess patient's respiratory effort.
- Check connections
- Plug machine in when not in use to charge battery.
- Check the patient's circulation
  - ? cold vs. warm
  - ? pale vs. pink
  - ? history of poor circulation
  - ? tape too tight on extremity
  - ? BP cuff or Arterial line present
- Check external light that might be interfering.
- Stop movement or select another area to monitor that is not moving.
- Try the machine on you to see if it is working

3. MONITORING VENTILATION

A monitor of ventilation is also very helpful during sedation – especially at deeper levels. While the pulse oximeter yields information about oxygen saturation, it does not give the status of the patient's ventilation – or exchange of CO_2. While these two physiologic variables often go together – this is not always the case. More importantly, the pulse oximeter has a significant "lag time" between the cessation of respirations (apnea) and the change in the pulse oximeter reading. In fact a child may be apneic for 30 seconds

(depending on size) before the oxygen saturation changes. The AAP guidelines on sedation are clear on this point. "The use of a precordial stethoscope or capnograph to aid in monitoring adequacy of ventilation is encouraged."[3]

PRECORDIAL/TRACHEAL STETHOSCOPE

Airflow through the upper airway can be measured directly or indirectly. The most common indirect method to assess airflow and airway patency is by auscultation over the trachea with a stethoscope (pretracheal stethoscope).

Gentle application of the pretracheal stethoscope over the trachea or upper chest allows the practitioner to assess airflow through the upper airway and detect partial obstruction or complete apnea. With inspiratory effort the degree of airway patency can be quantified by using the following 4-point stridor score[8]:

1. Normal breath sounds over the trachea by auscultation
2. Stridor detected by auscultation
3. Stridor audible without auscultation
4. No airway sounds detected (complete airway obstruction).

While the pretracheal stethoscope does not provide specific information regarding the location of an obstruction, it is particularly useful in determining the effectiveness of airway maneuvers in relieving obstruction and improving airflow. Similarly it is not a guarantee of adequate ventilation. Stridor scores of 2, 3 and 4 require airway repositioning. Pretracheal stethoscopes are accurate and inexpensive and particularly useful for brief procedures (e.g. bone marrow aspirates) performed with deep sedation. However depending on the procedure performed (e.g. MRI) they may not be particularly convenient to use.

CAPNOGRAPHY (END TIDAL CO_2 MONITORING)

Capnography refers to measuring the CO_2 level expired by a patient and processing that data graphically. Historically these monitors have used infrared wavelength absorption, Raman spectroscopy, or mass spectroscopy to measure CO_2. Their use has been standard in the operating room environment for years. CO_2 monitors are now widely available in very portable (handheld) forms using infrared technology. Capnographers are available from a variety of manufacturers and most use a "side stream" detection technique in which a small amount of gas is continuously sampled from the nasal cannula or inside of the mask, which the patient is breathing. The monitor measures the level of CO_2 in the gas and graphically displays the CO_2 content.

Capnography is a noninvasive monitoring tool that measures CO_2 concentration in exhaled gas, displayed continuously as a waveform through the respiratory cycle. Typically, this measurement is made using infrared light absorption based on the concept that CO_2 strongly absorbs infrared light with a wavelength of 4280 μm. CO_2 during expiration is typically divided into three phases (see figure below). During the first phase, the CO_2 concentration is low, reflecting the anatomical dead space in the trachea and large bronchi that are free of carbon dioxide. In Phase II, there is a rapid rise in carbon dioxide as alveolar gas begins to mix with dead-space gas. During Phase III, more and more of the alveoli empty and CO_2 concentration rises rapidly until a plateau level occurs, reflecting virtually all alveolar gas. Following Phase III, inspiration begins and CO_2 drops abruptly (Phase IV). The end tidal CO_2 concentration is the point just before inspiratory effort is initiated. Under normal conditions, the end tidal CO_2 is usually slightly less than the $PaCO_2$, with a normal difference of 2–5 mm/Hg. Note that this gradient may be considerably higher in situations where there is an increase in dead space.

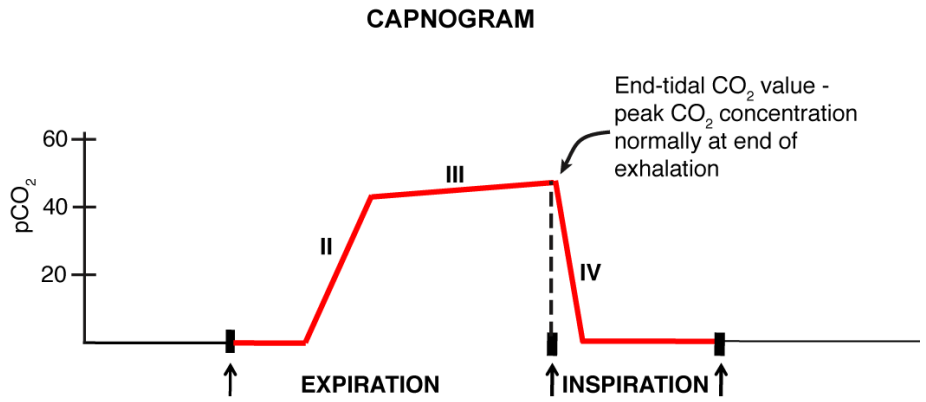
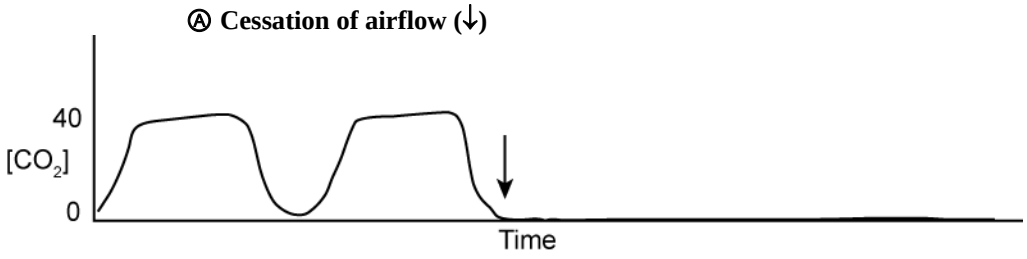


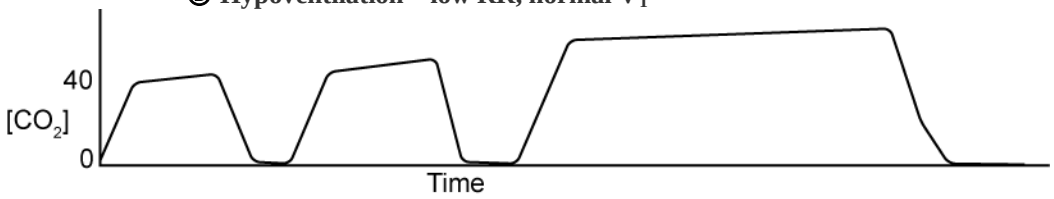
Figure: Components of the normal capnogram
I – (near zero baseline) Exhalation of CO_2 free gas contained in dead space.
II – (rapid sharp rise) Exhalation of mixed dead space and alveolar gas
III – (alveolar plateau) Exhalation of mostly alveolar gas
IV – (rapid sharp downstroke) Inhalation

During sedation, capnography is often used to assess real time breath-to-breath analysis of carbon dioxide with only a delay in detection of CO_2 changes of ~0.25 seconds. Consequently, acute changes in ventilation are rapidly detected by capnography. Indeed, capnography has been demonstrated to be superior to pulse oximetry in diagnosing apnea and reducing hypoxemic episodes.[29,30] Capnography is particularly important in locations where the medical team may be distant from the patient (e.g., during an MRI scan).

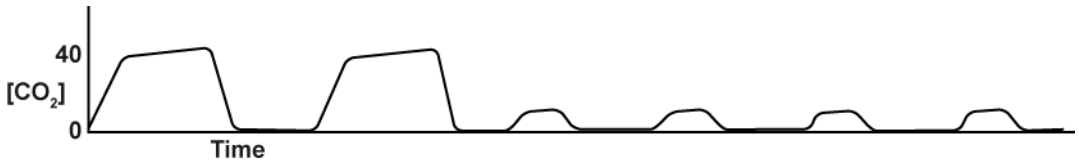
Capnograph tracings (see figures Ⓐ, Ⓑ and Ⓒ below)[31] - Complete cessation of airflow either secondary to apnea or complete airway obstruction (e.g. pharyngeal collapse or laryngospasm) results in absence of the CO_2 waveform, tracing Ⓐ. Consequently with capnography apnea can be detected as soon as it occurs.[32] Capnography can also be useful in detecting hypoventilation. The most common cause of an elevated end tidal carbon dioxide level during sedation is hypoventilation, tracing Ⓑ.・・・ Low respiratory rate and normal tidal volume is associated with a rising end tidal CO_2 that is accompanied by a rise in arterial CO_2 while maintaining the normal $EtCO_2$ - $PaCO_2$ gradient (~4-5 mmHg). Under these circumstances the $EtCO_2$ is a close approximation of the arterial CO_2. In contrast, a low $EtCO_2$ due to a greater dead space may accompany shallow respirations to tidal volume ratio (↑ V_D/V_T), tracing Ⓒ. This situation is accompanied by a wide $EtCO_2$ – P_aCO_2 value as the exhalation of dead space gas (low CO_2) "dilutes out" alveolar gas.[29]



Ⓑ **Hypoventilation – low RR, normal V_T**



Ⓒ **Hypoventilation – low V_T**



The capnograph can be used to confirm air exchange with each breath. Likewise rebreathing of CO_2 inside of a mask can be detected by the presence of CO_2 during the inspiratory phase of respiration. The absolute accuracy of the CO_2 level detected will vary with the monitor used, the type of oxygen delivery device, oxygen flow rates used, and the patient's pulmonary status. Therefore it cannot be considered completely reliable in providing an accurate CO_2 value.

Troubleshooting Capnography:

- If the capnograph is not recording any expired CO_2 first check to be sure that the child's airway is open and that there is respiratory effort. If no respiratory effort is present, initiate positive pressure ventilation immediately.
- If there appears to be respiratory effort but the end-tidal monitor is not working, check to be sure that the sampling line has not become disconnected or is not kinked.
- The sampling filter in the capnogram can be obstructed with water – and may need to be changed.
- Very high flows of oxygen in the mask or in the nasal cannula may "dilute" the CO_2 sample and give a very low or absent CO_2 reading.

4. MONITORING CARDIOVASCULAR FUNCTION

Electrocardiogram (ECG) and Blood Pressure:

The ECG is recommended by the AAP for deep sedation[3] and may be particularly useful when sedating for central line placement. The ECG provides information on the heart rhythm and rate – and can be used to validate the pulse oximeter value by correlating the heart rate by pulse oximeter to the ECG heart rate.

The AAP requires blood pressure monitoring for deep sedation.[3] Blood pressure monitoring is most helpful for deep sedation. During minimal or moderate levels of sedation the cycling of the cuff may be disturbing to the patient and may inhibit the effectiveness of sedation – many sedation providers omit blood pressure monitoring during sedation other than deep sedation or anesthesia.

5. MONITORING ACCORDING TO LEVEL OF SEDATION

(example of the University of Wisconsin monitoring guidelines)

Variable	Minimal Sedation	Moderate Sedation	Deep Sedation
	• Normal airway control • Normal respiratory responsiveness • Mild to minimal change in gross motor function • Normal level of awareness • Appropriate response to all stimuli	• Minimal to no loss of airway control • Minimal to mild alteration in ventilatory responsiveness (≤5% decrease in O_2 sat) • Mild to moderate impairment of gross motor function • Significant loss of orientation and impaired interaction with environment • Responds purposefully to light tactile and/or verbal stimulation	• Potential for partial or complete loss of airway control • Moderate alteration in ventilatory responsiveness (>5% decrease in O_2 sat) • Moderate impairment in gross motor function • Loss of orientation to and interaction with environment • Purposeful response to painful stimuli
Respiratory Effort	• Baseline and at 20 min	• Baseline and continuous • Document every 5 min	• Baseline and continuous • Document every 3–5 min
Heart Rate	• Baseline and at 20 min	• Baseline and continuous • Document every 5 min	• Baseline and continuous • Document every 3–5 min
***ECG**	• Not required	• Not required	• Recommended
Blood Pressure	• Baseline	• Baseline	• Baseline and every 3-5 min • Document every 3–5 min
Pulse Oximetry	• Not required	• Baseline and continuous • Document every 5 min	• Baseline and continuous • Document every 3–5 min
Ventilation	• Observation	• Observation	• Pretracheal stethoscope or $EtCO_2$ monitor recommended.
Mental Status	• Baseline and at 20 min	• Baseline and every 5 min	• Baseline and every 5 min
RN Attendance	• Immediately available	• Continuous	• Continuous
MD Attendance	• Readily available (on site)	• Immediately available	• Continuous

*not routinely used in MRI due to artifact

Recent guidelines emphasize the importance of being able to rescue a patient who inadvertently progresses to a deeper level of sedation.[3] Application of the AAP/ASA guidelines decreases risk of pediatric sedation. In a prospective quality assurance study of 960 sedation events risk reduction was associated with conductance of a pre-sedation risk assessment, adherence to hospital guidelines and avoidance of deep sedation.[33]

C. OVERVIEW OF DRUGS USED FOR SEDATION - GENERAL APPROACH TO PROCEDURAL SEDATION

The four primary goals of pediatric procedural sedation include maintaining patient safety, providing effective pain control, reducing anxiety and psychological stress, and promoting conditions conducive to successful performance of the procedure. To achieve these goals the sedation practitioner must have a clear idea of the desired clinical effects (i.e., the therapeutic window).

1. THE THERAPEUTIC WINDOW

The therapeutic window refers to the drug concentration associated with the desired clinical effects. It describes the relationship between the drug concentration and its therapeutic and adverse effects.

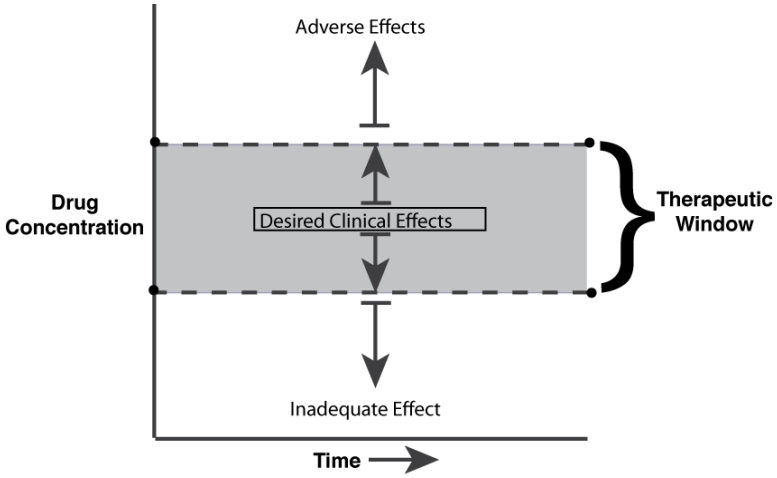
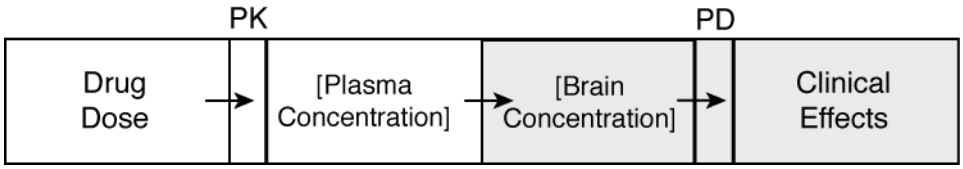


Figure: The Therapeutic Window

1. Concentrations of drug within the therapeutic window are associated with the desired clinical effect.
2. Drug concentrations above and below the "therapeutic window" result in inadequate and adverse clinical effects (e.g., hypoventilation), respectively.
3. Large interpatient variability exists between drug concentration and clinical response.
4. The goal is to administer the sedative drug that achieves the desired clinical effect ("right" drug) (pharmacodynamics) at the "right" time (pharmacokinetics).

2. PHARMACOKINETIC (PK) AND PHARMACODYNAMIC (PD) PRINCIPLES

A thorough understanding of the drug's pharmacokinetic and pharmacodynamic profile will promote safe and effective patient sedation. This next section will discuss the intimate relationship between the pharmacokinetics and pharmacodynamics of a sedative drug in achieving the desired effects.



PHARMACODYNAMIC FACTORS deal with "what the drug does to the body" (including both desired and adverse clinical effects). These effects are similar within a given class of drugs (e.g., opioids) and are dependent on the target organ and sedative receptor system. Common drug-receptor systems include the following:

- **Gamma-Aminobutyric acid ($GABA_A$) receptors** – $GABA_A$ receptors are ligand gated ion channels and function as the primary inhibitor neurotransmitter system in the central nervous system. Activation of the $GABA_A$ receptor results in Cl^- flux into the cell and subsequent hyperpolarization of the cell membrane. Many sedative and anesthetic drugs use the $GABA_A$ receptor system. For example, barbiturates and propofol bind to specific sites on the $GABA_A$ receptor and augment GABAergic neurotransmission.

- **Benzodiazepine (BNZ) receptors –** BNZ receptors are located on the $GABA_A$ receptor. BNZ agonists (e.g. midazolam, lorazepam) bind to BNZ receptors and enhance intrinsic GABA activity. Flumazenil is a competitive antagonist of the receptor.

- **G-Protein-Coupled receptors (GPCR) –** Agonists of the GPCR system reduce activity of adenyl cyclase and cause dephosphorylation of ion channels. This eventually results in activation of potassium channels and membrane hyperpolarization. Examples of GPCRs includes:
  1. **Opioid (μ_1,μ_2) receptors:** agonists: fentanyl, morphine; antagonist: naloxone
  2. **Central α_2 – receptors**: agonists: clonidine, dexmedetomidine

- **N-methyl-D-aspartate (NMDA) receptors –** The NMDA receptor is a ligand (e.g. glutamate) gated ion channel and functions as an excitatory neurotransmitter system. For example glutamate binds to the NMDA receptor, increases Na^+ and Ca^{++} flux into the cell and causes cellular depolarization. Ketamine blocks NMDA receptor neurotransmission by inhibiting Na^+ and Ca^{++} cell entry and preventing active depolarization.

PHARMACOKINETIC FACTORS deal with "what the body does to the drug." Pharmacokinetic properties typically distinguish drugs within a given class (e.g. fentanyl vs. morphine).

Intravenous Administration
For most rapidly acting intravenous sedatives onset of action and duration of effect is best explained by a (3) compartment model:[34,35,36,37]

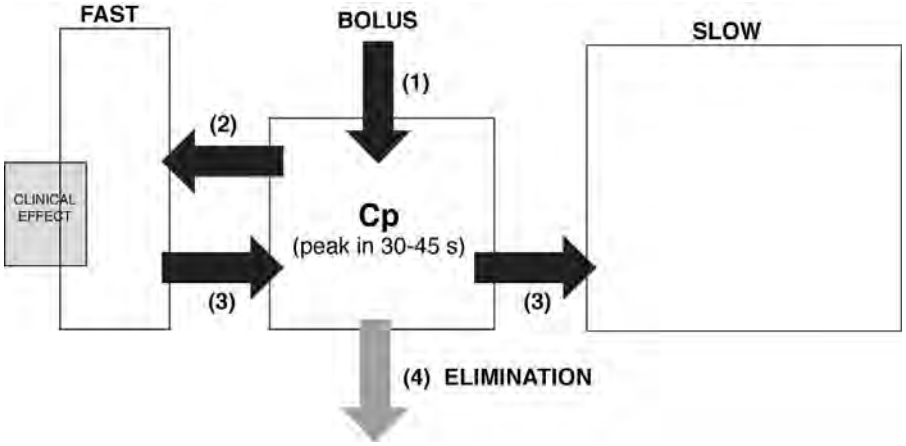


Figure: Distribution of rapid acting sedative drugs

(1) Following a bolus dose peak sedative drug plasma concentrations (Cp) occur in ~30-45 seconds.
(2) The sedative drug is first rapidly distributed to FAST compartments (e.g. brain) typically resulting in a rapid clinical effect.
(3) Sedative effect is terminated as the sedative drug is redistributed to SLOW compartments. Consequently, redistribution terminates clinical effect.
(4) Later, drug elimination occurs and is usually "unimportant" in determining the length of clinical action.

Bolus Dosing **(BD = Cp x VD)**
- Bolus dose (BD): A bolus dose of a drug is typically used to achieve a rapid clinical response. The appropriate dose of a sedative drug is determined by the desired plasma concentration (Cp) associated with the desired clinical effect and the volume of distribution (VD) in which the drug is dispersed.

- Physicochemical properties. Pharmacologic properties that are important in determining the speed and duration of action following bolus dosing include the following:
  (1) Blood flow (Vessel Rich Group, VRG) ≡ VRG organs (e.g. brain) receive the drug first because of high blood flow.
  (2) Protein binding ≡ only the non-protein bound portion of the drug crosses the cellular membrane and is active.
  (3) Degree of ionization (pKa) ≡ $A^- + H^+ \leftrightarrows AH$, unionized species cross the blood-brain barrier and are pH dependent.
  (4) Lipid solubility ≡ fat solubility is the most important physicochemical property of sedative drugs that influences the speed of action and duration of effect. Highly lipid-soluble drugs penetrate and depart the brain quickly. Very lipid-soluble drugs typically have a large V_D.

Continuous Infusion Dosing **(CI=Cp x CL)**

- Constant Infusion (CI): The infusion rate of a drug is determined by the desired Cp and the drug's clearance (CL).
- While a bolus dose is administered to achieve a rapid clinical response, continuous infusions may be used to maintain the target plasma concentration and desired clinical response. Propofol is a good example of using a continuous infusion to maintain the desired clinical response.
- Clearance: Clearance is measured as volume per unit time and is usually expressed as the "amount of blood cleared" of drug over time. The liver and kidneys are the principle organs of drug clearance. Drugs with high clearance values require high infusion rates to maintain the Cp and desired clinical effect.

Other routes of Administration

Oral

For a number of sedatives the oral route is a convenient method of administration. Problems with oral dosing however include first pass hepatic metabolism, inconsistent onset of clinical effect and inability to titrate. Oral doses are often considerably greater than intravenous doses and may result in prolonged clinical effect. Because of first pass hepatic metabolism "active" metabolites may predominate with oral administration (e.g. norketamine) following ketamine administration. Examples of sedatives commonly given orally include chloral hydrate, midazolam and ketamine.

Rectal

Rectal administration has advantages over the oral route in patients with nausea and vomiting, and who refuse medications by mouth. In addition first pass hepatic metabolism is partly avoided due to systemic drug absorption that occurs in the distal portion of the rectum. Absorption in the upper rectum and colon is through the portal system and go through first pass hepatic metabolism. One significant disadvantage of rectal administration is the general lack of acceptability in children over 3 years of age. Midazolam and ketamine are examples of drugs that can be given rectally.

Intranasal

Intranasal absorption of drugs occurs directly into the systemic circulation, avoiding first pass hepatic metabolism. Consequently drug doses are considerably less than the oral route and clinical effect is more rapid. While intranasal administration is typically easy, it may not be well tolerated by some children. Examples of sedatives that can be given intranasally include midazolam, ketamine and dexmedetomidine.

3. CHOOSING A SEDATIVE BASED ON PHARMACODYNAMICS AND PHARMACOKINETICS

Four basic questions can assist the practitioner in choosing the most appropriate sedative for the patient and procedure:

1. What are the DESIRED CLINICAL EFFECTS?
2. HOW FAST are the effects desired?
3. HOW LONG are the effects desired?
4. What drug effects are NOT DESIRED or CONTRAINDICATED?

Give the "Right Drug" at the "Right Time" approach makes use of the pharmacodynamic and pharmacokinetic properties of an individual drug or drug combination. Optimal use of the pharmacologic effects of a sedative drug is depicted in the figure below. In this example an analgesic agent (e.g. fentanyl) is combined with a sedative hypnotic (e.g. propofol) for an invasive procedure (bone marrow aspiration). Both drugs are given at the appropriate time and achieve the desired plasma concentration and clinical effect (shaded area) during the painful procedure. In addition an anxiolytic (e.g. midazolam) is administered as a premedicant prior to the procedure.

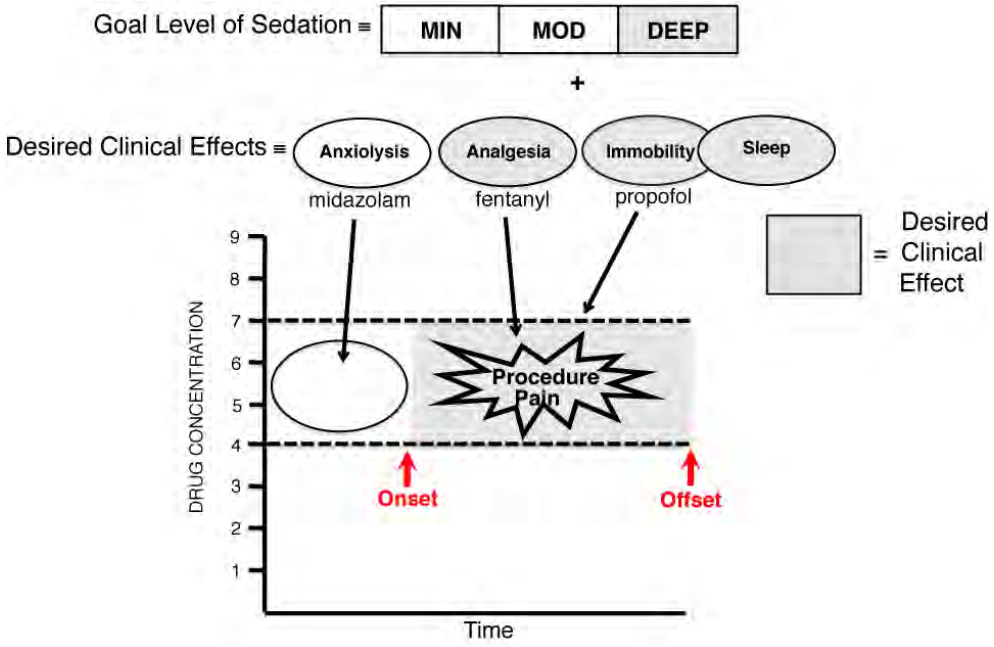


Figure: Integrating pharmacodynamics and pharmacokinetics to achieve the desired clinical end point.

In the figure below two examples of inadequate procedural sedation are shown. The first, "pharmacokinetic failure", is an example of giving an analgesic, such that the peak analgesic effect occurs after the painful procedure is completed "right drug at the wrong time". A classic example is performing a fracture reduction immediately after intravenous morphine (a slow acting analgesic). The second example is one of "pharmacodynamic failure" in which an inappropriate drug (i.e. a drug without analgesic properties) is given for a painful procedure.

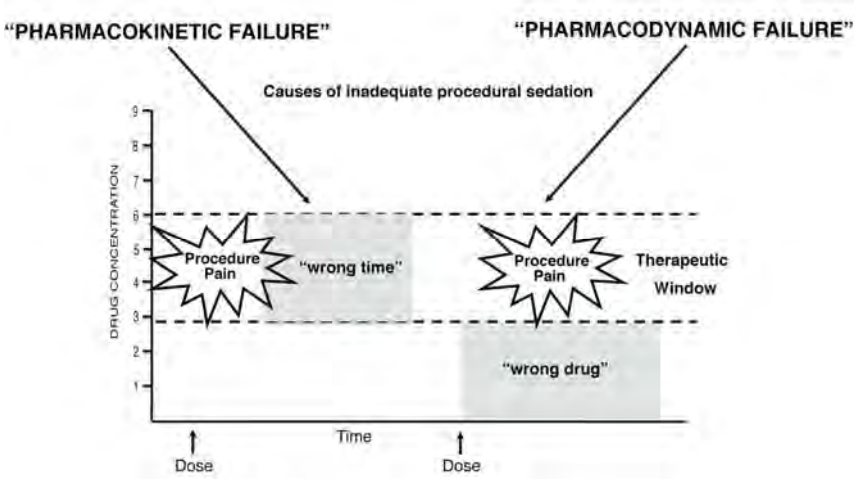
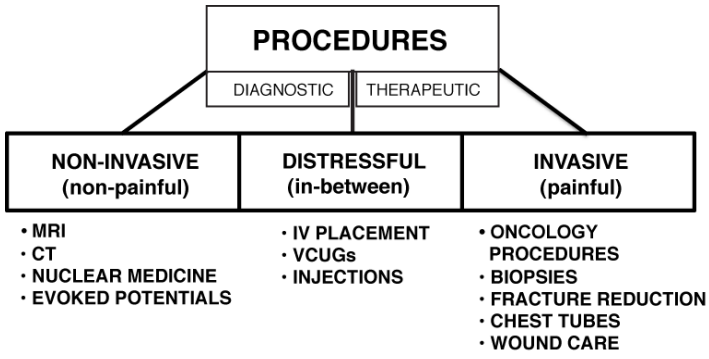


Figure: Basic causes of inadequate procedural sedation

4. THE PROCEDURE

In general procedures are either diagnostic, therapeutic or both. An example of both a diagnostic and therapeutic procedure is a lumbar puncture for administration of intrathecal chemotherapy and collection of cerebral spinal fluid. Diagnostic and therapeutic procedures can be further categorized as Invasive and Noninvasive. In this course a third category termed Distressful or Minimally Invasive is intended to refer to "in-between" procedures not traditionally falling into either Invasive or Noninvasive categories, and accompanied by physical or emotional distress by the patient (see figure below).



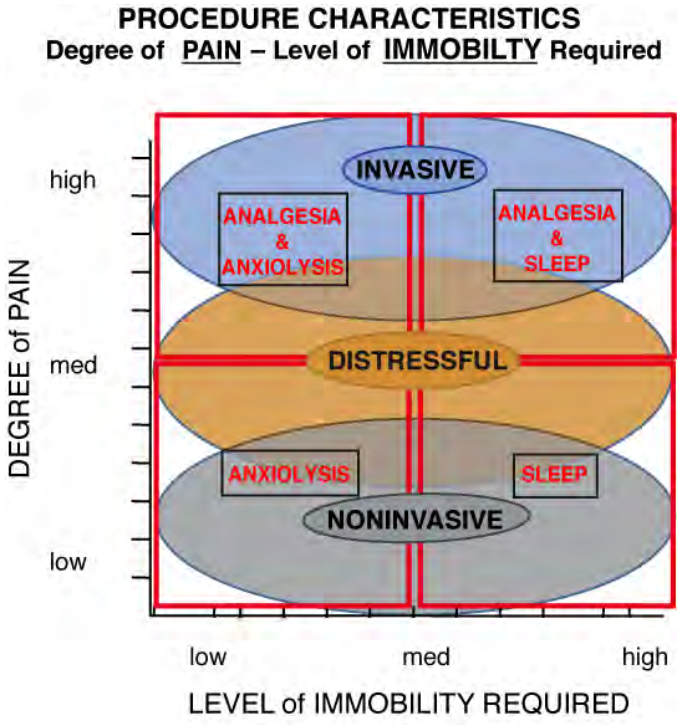
STEDMAN'S Medical Dictionary, 27th Edition

1. Invasive (Painful) Procedures ≡ "procedure that requires insertion of a device through the skin or body orifice."
   Examples of the more common painful procedures performed on children are listed in the diagram above. Invasive oncology procedures are among the most common painful procedures performed in children (e.g. lumbar punctures, bone marrow aspirates/biopsies). While it is not the intent of this course to focus on painful cancer procedures, they do illustrate several important aspects of effective procedural sedation and pain control in children:
   - Invasive procedures are considered one of the most stressful parts of pediatric cancer treatment for patients and families.
   - Initial poorly controlled procedural pain is associated with the development of anxiety related disorders in children and diminished analgesic effects in subsequent procedures.[38]

- The American Academy of Pediatrics (AAP) recommends that procedural pain management be part of the “front line” treatment in children with cancer. [39]

2. Noninvasive (Non-Painful) Procedures ≡ “a procedure that does not require insertion of a device through the skin or a body orifice.”
   Some noninvasive diagnostic studies require a high level of patient "immobility" to be satisfactorily completed and include Magnetic Resonance Imaging (MRI) scans, Computerized Tomography (CT) scans, Nuclear Medicine scans, Pulmonary Function Test (PFTs) and Evoked Potentials. These studies often require Deep Sedation for successful completion.
3. Distressful Procedures (Minimally Invasive) ≡ a procedure that results in mental or physical suffering or anguish.”
   Some procedures do not fit neatly into Invasive or Noninvasive studies. Consequently the designation “Distressful Procedures” is used in this course to describe a number of procedures that are “in between” and historically may not have “required” sedation but are accompanied by significant distress. Examples include foley catheters, voiding cystourethrograms (VCUG)[40,41] and injections of various sorts.

Further defining the characteristics of the procedure assists in determining the most appropriate sedative agent. Based on the degree of **procedural pain** and amount of **procedural immobility** required to complete the procedure, general categories of procedures can be defined. The diagram below categorizes procedures in terms of degree of pain and levels of immobility.



Characteristics identified by the oval areas categorize procedures in general terms based on degree of pain. Common clinical endpoints (e.g. anxiolysis, analgesia) are further identified in the boxes. Noninvasive procedures typically require sedative-anxiolytics or under circumstances of high immobility, sedative-hypnotics. Distressful procedures require varying degrees of pain or anxiety control based on the procedure and patient. Invasive procedures are best managed with analgesic agents and when high levels of immobility are required combination analgesics – anxiolytics or hypnotics may be necessary.

D. SEDATIVE DRUGS (see Appendix for sedative drug summary)

The following section discusses the most common sedative drugs used in pediatric procedural sedation practice. It is by no means an exhaustive list of sedative drugs that can or have been used in children. From a historical standpoint, hypnotic agents like chloral hydrate and pentobarbital stand out as "sleepers" that have stood the test of time. Some of sedatives used in the 70's and 80's like paraldehyde, Demeral/Phenergan/Thorazine (the DPT cocktail) and a shot of brandy will not be commented upon except perhaps to make the point that sedation practice has come a long way.

This section is divided into 3 parts based on the predominant characteristic feature of the sedative drug:

Sedative-Anxiolytics – Drugs that reduce anxiety
Sedative-Hypnotics – Drugs that result in sleep
Sedative-Analgesics – Drugs that have analgesic properties

1. PRIMARY SEDATIVE – ANXIOLYTIC DRUGS

Sedative – anxiolytic drugs are used to make children "more workable" and comfortable. Benzodiazepines are the most common drugs used in this category. Benzodiazepines are particularly effective for noninvasive procedures or distressful procedures that do not require high levels of immobility. They are also useful as premedicants and as adjuncts with analgesics. Alone, benzodiazepines are not analgesics and are poor hypnotics.

- **BENZODIAZEPINES (BNZ):**

(1) DIAZEPAM, MIDAZOLAM, LORAZEPAM

Benzodiazepines enhance gamma-aminobutyric acid (GABA) neurotransmission by binding to specific BNZ receptors on the $GABA_A$ receptor complex. They enhance chloride flux across ligand-gated ion channels, resulting in membrane hyperpolarization and inhibition of the action potential.

As a class, the benzodiazepines midazolam, diazepam and lorazepam have very similar clinical effects. However, midazolam's physicochemical and pharmacokinetic properties distinguish it from diazepam and lorazepam and include: a water soluble preparation, less irritation during intravenous administration, greater compatibility with other drugs, faster recovery (particularly compared to lorazepam) and a shorter elimination half life. The table below lists doses, onset of action and duration of intravenous diazepam, midazolam and lorazepam.

Benzodiazepine	Dose	Repeat Dose	Onset	Duration
Diazepam	0.1-0.15 mg/kg	0.05-0.1 mg/kg q 3-5 min	<60 sec	15-30 min
Midazolam	0.05-0.1 mg/kg	0.05 mg/kg q 3-5 min	<60 sec	15-30 min
Lorazepam	0.05 mg/kg	.025-0.05 mg/kg q 10-15 min	2-3 min	1-2 hrs

The most commonly used benzodiazepine for pediatric sedation is midazolam – consequently this section will focus on the use of this particular drug.

(2) MIDAZOLAM

Midazolam is a short acting, water-soluble benzodiazepine devoid of analgesic properties. The drug has become particularly popular because of its short duration, and predictable onset. It is effective in eliminating the stress response largely by binding with $GABA_A$ receptors to inhibit spinal afferent pathways. This results in skeletal muscle relaxation, amnesia, and anxiolysis.

Oral Midazolam:

Although originally formulated for intravenous use, the same medication used orally has proven very successful in producing light sedation, anxiolysis and amnesia.[42,43,44,45,46] The recommended oral dose is 0.3-0.75 mg/kg, with an onset of sedation in approximately 15 minutes and a rapid offset approximately 30 minutes after the peak effect is noted. It is metabolized in the liver- undergoing a large first pass effect and has a beta elimination half-life of 106 +/- 29 minutes. Unfortunately, the drug has a very bitter taste that is difficult to disguise. Several strategies including dilution in cola syrup, apple juice with sweeteners, ibuprofen syrup, or liquid acetaminophen have been described. Flavored oral preparations are now available. Allowing self-administration through a prefilled syringe in a comforting environment (parent's arms) has met with the most success in these authors' experience.

Respiratory depression is rare with oral administration of midazolam.[42] As a general rule, this medication and mode of administration comes the closest of any of the current sedatives available to providing true minimal sedation - providing a sedated yet arousable and cooperative patient at the indicated doses. One of the most desirable side effects is the anterograde amnesia that is produced. The degree of amnesia will vary with the age of the patient, the invasiveness of the procedure and the dose given.[43]

Recommended Use: Oral midazolam is most useful as a sole agent for children who will drink liquid medication. Anxiolysis and cooperation are excellent as an anesthetic premedication at doses of 0.5 mg/kg[45,46] and for minor invasive procedures such as intravenous catheter placement and voiding cystourethrograms.[47,48,49] Administration of a local anesthetic may provide the analgesia necessary to allow a painful procedure to be performed.

Rectal Midazolam:

Midazolam may be administered rectally at doses of 0.3-0.75 mg/kg. A dose of 0.3 mg/kg has been shown to give reliable levels of sedation with a mean time of 16 minutes to maximal blood level.[50] Rectal administration is generally not as well tolerated in children > 3 years of age. After thirty minutes, blood levels were generally low but sedation and anxiolysis effects remain.

Nasal Midazolam:

Midazolam may be given by the intranasal route at doses of 0.2-0.4mg/kg. Onset time is intermediate between the oral and intravenous routes of administration (10-15 minutes). The effectiveness of this route of administration is well established as a premedicant for anesthesia but its use is limited by burning on application to the nasal mucosa which most children find very objectionable, as well as the bitter taste of midazolam reaching the oropharynx.[51] Adverse effects including respiratory depression and synergy with opioids are similar to those mentioned above.[44]

Recommended Use: For sedation and anxiolysis in young children who either refuse or cannot take an oral dose of midazolam. Onset is reliable but most children will only accept this route of administration once.

The table below is a summary of oral, rectal and nasal administration of midazolam

Route	Dose	Clinical Onset	(+) Attributes	(-) Attributes
Intranasal	0.2-0.4 mg/kg	10-15 min	fast onset	irritating
Rectal	0.3-0.75 mg/kg	15-20 min.	age < 3 yo	not older children
Oral	0.3-0.75 mg/kg	15-30 min	easy delivery	variable onset, bad taste

Table: Summary of enteral midazolam administration – route, dosing, clinical onset and positive (+) and negative (-) attributes.

Intramuscular Midazolam:
Midazolam may be given as an intramuscular bolus of 0.08-0.1 mg/kg. Good sedation and cooperation scores were recorded at 15 minutes after this dose in one study.[52] Persistent sedation is minimal 60 minutes after the dose.

Recommended Use: Midazolam gives reliable sedation after intramuscular dosing - a useful alternative for children who will not accept oral medications, particularly where residual sedation is a concern.

Intravenous Midazolam:
Intravenous midazolam is highly lipid soluble and redistributes rapidly. Consequently intravenous midazolam can be titrated to effect with fractionated doses of 0.05-0.1 mg/kg that may be repeated at intervals of 3 to 4 minutes. As opposed to the oral route of administration, intravenous midazolam reaches peak effect in 2 to 3 minutes. Slow intravenous administration is recommended with close observation for respiratory depression. When combined with intravenous opioids for painful procedures, midazolam has potent sedative effects and the use of cardiorespiratory monitoring is imperative. A maximum intravenous dose of 0.05 mg/kg has been recommended when combining the drug with narcotics.

Anterograde amnesia is even more prominent than when the drug is used orally. Slurred speech has been shown to coincide with the onset of anterograde amnesia. As mentioned in the introduction, the value of amnesia and anxiolysis cannot be underestimated in the performance of painful procedures in children.[53] In a double blind, randomized cross over study most children undergoing invasive oncology procedures preferred midazolam to fentanyl for sedation.[53] Patient preference was felt secondary to amnesia for the procedure with midazolam (~90%).

Certain underlying conditions or medications may prolong the effects of midazolam. Heparin decreases protein binding and increases the free fraction. Hepatic metabolism is inhibited by cimetidine, which prolongs the elimination half-life. Patients in renal failure may have three times the free fraction of the drug secondary to decreased protein binding.[54]

Recommended Use: Intravenous midazolam is an excellent agent for sedation and anxiolysis in patients for minor procedures when an intravenous line is in place. It provides complementary sedation for patients receiving opioids for very

painful procedures due to synergy but extreme caution is warranted when combining the drugs due to respiratory depression.

- **NITROUS OXIDE**

Nitrous Oxide (N_2O) is a colorless, odorless gas that has both analgesic and anxiolytic effects. The drug must be delivered with oxygen to avoid a hypoxic gas mixture. This may be accomplished though the use of flow meters from separate sources or through the delivery of a fixed 50% mixture of N_2O/oxygen (Entonox). The drug may be delivered alone at concentrations of 30-70% for mild to moderately distressful and painful procedures or in combination with a mild sedative at lower concentrations for similar effect.[55] Higher N_2O concentration of 70% as the sole sedating agent was found to be safe in a series of 762 pediatric procedures.[56] Onset of sedation and analgesia occurs in minutes and is terminated rapidly when the gas is discontinued. Nitrous Oxide has minimal cardiovascular and respiratory effects when not combined with a potent sedative or opioid. Studies in large groups of patients have failed to show any significant risk of cardiopulmonary depression when nitrous oxide is used at the concentrations cited here.[57] Indeed N_2O concentrations of 30-50% are considered Minimal Sedation by the AAP.[3]

Cautions when using the drug include the possibility of providing a hypoxic mixture of gas to the patient if equipment fails. Deep sedation is possible with high concentrations or when combined with opioids – this may be avoided by insisting on self-administration of higher than 30% concentration of N_2O. There is a slight increase in nausea and vomiting associated with use of nitrous oxide but airway reflexes are reliably maintained. If any inhalational agent is to be used, Occupational Safety and Health Administration (OSHA) guidelines for scavenging and room air turnovers must be met. This requirement may make the use of N_2O impractical except in dedicated rooms where such equipment is present.

Recommended Use: Nitrous oxide is useful for brief distressful and painful procedures like intravenous catheter placement[58], injections[59] and urologic procedures[60] and may be combined with a mild sedative (e.g. midazolam). Expensive equipment and ventilation apparatus required for delivery may limit its widespread use.

2. PRIMARY SEDATIVE – HYPNOTIC DRUGS ("SLEEPERS")

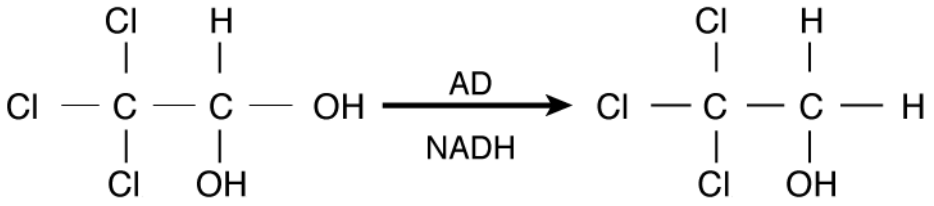
Sedative – hypnotic drugs are primarily used to facilitate the onset of sleep. They are particularly effective for noninvasive procedures requiring a high level of immobility.

- **CHLORAL HYDRATE**

Historically chloral hydrate has been one of the most widely used hypnotic agents in children. It is generally considered a safe and effective agent, particularly in children under 2 years of age. One of the main advantages of chloral hydrate is the only mild to moderate degree of respiratory depression following administration.[61] Respiratory depression is most marked when the drug is combined with opioids or other sedatives. In addition, certain patient populations are at higher risk of having respiratory depression and oxygen desaturation following chloral hydrate administration. Examples of higher risk patient populations include children with bronchiolitis[62], patients with obstructive sleep apnea[63] and infants.[64] In a retrospective study of chloral hydrate sedation in term and preterm infants the overall incidence of oxygen desaturation (SpO2 < 90%) during the procedure was ~ 20%. In addition risk factors for oxygen desaturation postprocedure were younger chronological age (< 2 months) and a lower body weight (~4 kg). Isolated mild oxygen desaturations occur in approximately 5% of children receiving standard doses of chloral hydrate.[65] Other issues with chloral hydrate includes agitation, often occurring prior to the child falling asleep, vomiting and

unpalatability. The use of chloral hydrate for procedural pain is limited by the fact that it lacks any analgesic properties.

Chloral hydrate is 2,2,2-trichloroacetaldehyde, a halogenated hydrocarbon that is metabolized by alcohol dehydrogenase (AD) to trichloroethanol, the major active metabolite. Trichloroethanol has an elimination half-life of approximately 8-11 hours. Scheduled administration of chloral hydrate more than 1 to 2 times a day may result in accumulation of trichloroethanol.



Choral Hydrate **Trichloroethanol (TCE)**

Clinical effectiveness is multifactorial. It is particularly effective for nonpainful procedures requiring sedation or sleep in children younger than 2 years of age who do not require an intravenous catheter. Some practitioners recommend sleep deprivation for children prior to giving chloral hydrate. Chloral hydrate should be given in a quiet, calm and dimly lit environment to be most effective. Chloral hydrate is well established as a sedative for painless procedures such as CT scans, MRI scans and echocardiograms. Success rates for both CT and MRI are typically greater than 85% and in organized sedation services success rates exceed 95%.[66,67,68,69,70,71] Chloral hydrate at 80 mg/kg results in effective sedation for ultrasound studies like echocardiography with few significant adverse events, although monitoring should be planned for at least moderate sedation.[72] Usefulness in painful procedures is limited by patient movement and agitation that occurs during a painful procedure even when the child may appear to be very sedated. The long elimination half-life of chloral hydrate (trichloroethanol) often is an indication for prolonged supervision prior to discharge.

Recommended Use: Doses of chloral hydrate are typically 50-75 mg/kg either orally or rectally. For CT scans, 75-100 mg/kg has been used with a maximum dose of 2 grams.[65] Repeat doses of 20-25 mg/kg at 20-25 minutes following the first dose can be given for children who do not fall asleep within that time period. Usually induction times are 15-25 minutes, however induction times may be delayed, with peak effect taking as long 60 minutes. Recovery time is typically 60-120 minutes, however the drug can result in prolonged sedation, particularly in infants.[43,64]

- **BARBITURATES**

Barbiturates are potent sedative, hypnotic, anesthetic agents with strong anticonvulsant properties. The primary mechanism of action is through the $GABA_A$ receptor. As a class the structure of barbiturates is based on the barbituric acid ring. Various substitutions on the barbituric acid ring confer different clinical effects including speed of action, hypnotic potency and anticonvulsant effects (see figure below). Barbiturates do not have analgesic properties. Most sedation experience is with pentobarbital and to a lesser degree methohexital.

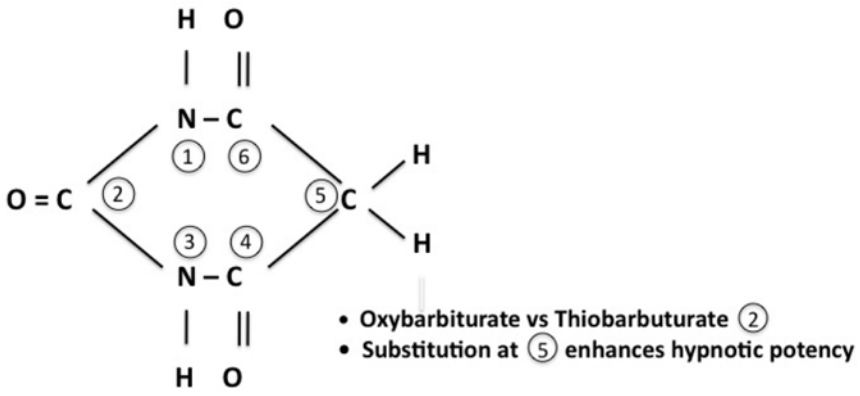


Figure: The barbituric acid ring

(1) PENTOBARBITAL

Pentobarbital is an oxybarbiturate and is one of the most frequently used barbiturates for pediatric sedation. It is a very good hypnotic and very effective for nonpainful procedures requiring a high level of immobility such as CT and MRI scan.[66,73] Pentobarbital has respiratory depressant effects that are generally well tolerated in otherwise healthy children. While pentobarbital has negative iontropic and vasodilator properties, there are few clinically significant cardiovascular effects in otherwise healthy individuals when given for sedation purposes. Hemodynamic effects are most pronounced when the drug is given rapidly and in patients with hemodynamic instability and hypovolemia. During induction with pentobarbital for sedation, excitatory phenomena such as agitation are not uncommon.

Recommended Use:

Intravenous: Most experience with pentobarbital is with intravenous administration. Initial doses of pentobarbital are 2-4 mg/kg intravenously over 30-45 seconds. A 1-2 mg/kg dose can be repeated in 5-10 minutes after the first dose if the patient is not asleep. Induction times are typically within 1-2 minutes with recovery times of approximately 60 minutes. At the doses listed above, pentobarbital has a greater than 95% success rate for both MRI and CT scans.[66,73,74] However, oxygen desaturations are not uncommon occurring in approximately 5% of patients. Recovery may be prolonged particularly when compared to propofol and at times accompanied by agitation.[75,76]

Oral: Oral doses of pentobarbital (4-5 mg/kg) have been shown to have a high success rate for noninvasive imaging studies like echocardiograms and MRI and CT scans.[77,78] Safety, efficacy and recovery times are similar to chloral hydrate.

(2) METHOHEXITAL

Methohexital is an oxybarbiturate with clinical effects similar to pentobarbital. Excitatory phenomena are more common however. Rectal administration at doses of 25-30 mg/kg have similar efficacy and faster recovery times to chloral hydrate for CT scans and MRI scans.[79] Progression to deep sedation and excitatory phenomena are disadvantages of methohexital.

- **CENTRAL ALPHA-2 ADRENERGIC AGONISTS**

Central α-2 agonists bind to pre and postsynaptic central alpha-2 receptors located primarily in the locus coeruleus. Activation of the receptor decreases activity of adenyl cyclase and results in dephosphorylation of ion channels associated with the alpha-2 receptor. Potassium channels are activated resulting in potassium efflux out of the cell

and membrane hyperpolarization. In addition calcium flux into the cell is inhibited. Ultimately adrenergic output is reduced. Desirable clinical effects include anxiolysis, "natural" sleep and little respiratory depressant effects. Central α-2 agonists are not amnestics.

(1) CLONIDINE

Clonidine has been used as an oral preanesthetic in children for years. At doses of 3-5 mcg/kg clonidine results in sedative and anxiolytic effects similar to oral midazolam.[80,81] Clonidine has been demonstrated to be effective for sedating children with autism for EEG.[82] Disadvantages of oral clonidine is slow onset (> 30 minutes) and prolonged duration, often greater than 90 minutes.[46]

(2) DEXMEDETOMIDINE

Dexmedetomidine is a highly selective central alpha-2 adrenergic receptor agonist that has been found to have both sedative, anxiolytic, hypnotic and analgesic properties. Compared with clonidine, dexmedetomidine selectively binds to α-2 adrenergic receptors with an alpha-2 to alpha-1 adrenergic receptor ratio of approximately 1600:1 (7-8 times higher than clonidine). Dexmedetomidine has a number of desirable clinical effects that includes "cooperative sedation", a hypnotic state that simulates natural sleep and some analgesic properties. Dexmedetomidine has significant effects on sinus and atrioventricular node function.[83] Consequently dexmedetomidine may cause fairly significant bradycardia on intravenous administration.

Dexmedetomidine has a number of advantages over more commonly used hypnotic agents. Although it produces sedative, analgesic, and anxiolytic effects, unlike other sedatives, it results in less respiratory depression. Because of the bradycardia and hypotension that can occur with dexmedetomidine, care should be taken when administering this drug to patients who are volume depleted, and vasoconstricted as dexmedetomidine can cause hypotension and bradycardia in this patient population. Dexmedetomidine should be avoided in patients with sinus or atrioventricular nodal block and in those taking digoxin.

Recommended Use: Dexmedetomidine can be given intranasally, submucosally, orally[84] and intravenously.[85,86] When given intravenously, dexmedetomidine is given as a bolus dose of 0.5-2 mcg/kg over 5-10 minutes to avoid bradycardia and hypotension followed by an infusion of 1 to 2 mcg/kg/hr.[85,86] Clinical onset is usually within 5-10 minutes. Dexmedetomidine has been demonstrated to be effective as a sole agent for noninvasive procedures such as MRI scans, with potential advantages in children with autism.[87,88] In addition dexmedetomidine may be particularly useful for children requiring sedation for EEG. In a recent study dexmedetomidine did not impair EEG interpretation and resulted in an EEG pattern similar to Stage II sleep.[89]

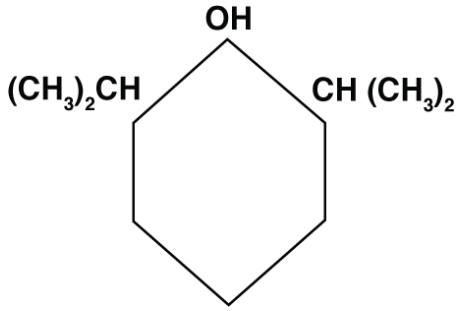
Absorption of dexmedetomidine by the nasal buccal route is 82% when compared to intravenous administration. Nasal dexmedetomidine (1 mcg/kg) administration has been shown to be a well tolerated and effective route for sedation in children.[90] Sedation onset is slow, typically taking 30 to 45 minutes. One other disadvantage is the potential for prolonged recovery.

- **ETOMIDATE**

Etomidate is an imidazole compound increasingly used as a hypnotic agent for pediatric procedural sedation in the emergency department.[91] In a manner similar to barbiturates and propofol, etomidates mechanism of action is via the $GABA_A$ receptor. Following a single intravenous dose onset of action is in ~ 1 minute with a duration of 10-15 minutes. In a report from the Pediatric Sedation Research Consortium etomidate at

doses of ~ 0.3 mg/kg was superior to pentobarbital (4 mg/kg) for CT scans in terms of both recovery times and adverse events.[74] Similarly, etomidate (0.2 mg/kg) with fentanyl was more effective and resulted in faster recovery times than a midazolam-fentanyl combination for pediatric fracture reduction.[92] The incidence of adverse events were similar between groups. Overall etomidate is an effective hypnotic agent for noninvasive procedures as well as invasive procedures when combined with an analgesic. Disadvantages include pain at the injection site, myoclonus, vomiting (~ 5%) and transient adrenocortical dysfunction following administration.[93,94]

- **PROPOFOL**



2,6 - Diisopropylphenol

Propofol is 2,6 diisopropylphenol, a phenol derivative with sedative, hypnotic and anesthetic properties. Because it is only slightly soluble in water, the drug is dissolved in a solution of soybean oil, typically in a concentration of 10 mg/ml. The nature of the solution requires the drug be handled in a sterile manner and be used quickly once it is open. For many noninvasive procedures such as CT scan and MRI scan, propofol has replaced drugs like chloral hydrate and pentobarbital in some institutions because of its desirable pharmacological effects that include a rapid onset of action, quick recoverability and easy titratability.[95,96,97] Propofol's primary mechanism of action is through the $GABA_A$ receptor. Through this mechanism propofol results in neuronal cell membrane hyperpolarization, inhibition of the action potential and a reduction in cell activity.

Propofol's clinical effects are dose dependent. Propofol has antiemetic, anxiolytic, amnestic, hypnotic and anesthetic properties. However it does not have analgesic effects. Adverse clinical effects of propofol include significant respiratory depression that is accompanied by a reduction in airway tone and control.[8,98] In addition there is a dose dependent decrease in ventilatory response to carbon dioxide that is typically accompanied by a reduction in tidal volume. In a recent study of 49,836 propofol sedations from the Pediatric Sedation Research Consortium oxygen saturation < 90% and central apnea/airway obstruction occurred 154 and 575 times per 10,000 administrations, respectively.[99] Cardiovascular effects are usually well tolerated in healthy children with decreases in blood pressure and heart rate of 10-20% being common. As noted earlier, propofol is a potent central nervous system depressant that has occasionally been used as an anticonvulsant. Propofol causes pain on injection, which may be prevented by administering a small dose of lidocaine (1 mg/kg intravenous or placing 1 mg of lidocaine per 1 ml of propofol) or administering propofol through a large vein.

The three properties of propofol that make it such a useful sedative-hypnotic are high lipid solubility, large volume of distribution and high metabolic clearance. In fact clearance of propofol exceeds hepatic blood flow. Propofol is metabolized by the liver

through glucuronidation pathways to inactive conjugated metabolites. It is highly protein bound. Its pharmacokinetics is summarized best by a 3-compartment model. Note: Infants have a larger volume of distribution and a greater metabolic clearance than older children. Consequently bolus doses required to achieve clinical effect is higher in infants. Similarly because the metabolic clearance is higher in infants, continuous infusions rates are greater.

Recommended Use: Propofol can be administered by either bolus dosing or bolus dosing followed by a continuous infusion. Because of propofol's short duration, procedures exceeding 15 to 20 minutes are often best managed by a bolus dose followed by continuous infusion to maintain the desired plasma concentration and clinical effect. As noted above onset of action is extremely rapid and induction of sedation or anesthesia may be achieved with 2-3 mg/kg in 95% of patients within 60-90 seconds. Typical induction doses for sedation include infusing propofol at 0.5-2 mg/kg/min until the child is asleep. Infusions of 100-150 mcg/kg/min maintain sleep in close to 100% of patients. Doses of propofol following induction can be used at 0.5-1 mg/kg if the patient awakens.

Noninvasive Procedures: Propofol is particularly effective as a sole agent for noninvasive radiologic procedures. For MRI and CT scans infusions of 100-150 mcg/kg results in a very high success rate.[24,95,96] However airway compromise and oxygen desaturations are not uncommon, typically occurring in 5-15% of patients.

Invasive Procedures: Propofol is also very effective either as a sole agent or combined with opioids/ketamine for brief painful procedures. As a single agent propofol is effective for invasive oncology procedures[100,101] and gastrointestinal procedures.[102] Use of propofol with fentanyl for invasive oncology procedures results in lower doses of propofol overall and fewer adverse effects.[103] Evidence of the superiority of an opioid – propofol combination may be due to synergism when these agents are used together.[104,105] Propofol is an ideal agent for brief periods of deep sedation. In expert hands propofol is very effective and has minimal significant adverse effects.

Note: Because anesthesia with its complete loss of airway reflexes, respiratory depression and cardiovascular depression can be induced so rapidly with propofol, many hospitals limit its use to anesthesia personnel. The role of this drug in the intensive care unit and emergency department remains to be defined – clearly only individuals skilled in airway management should be administering the drug.

3. PRIMARY SEDATIVE – ANALGESIC DRUGS

Primary sedative analgesic drugs are drugs that are particularly useful for painful procedures. Analgesic agents may occasionally be combined with anxiolytics or hypnotics to enhance analgesic effects.

- **OPIOID AGONISTS**

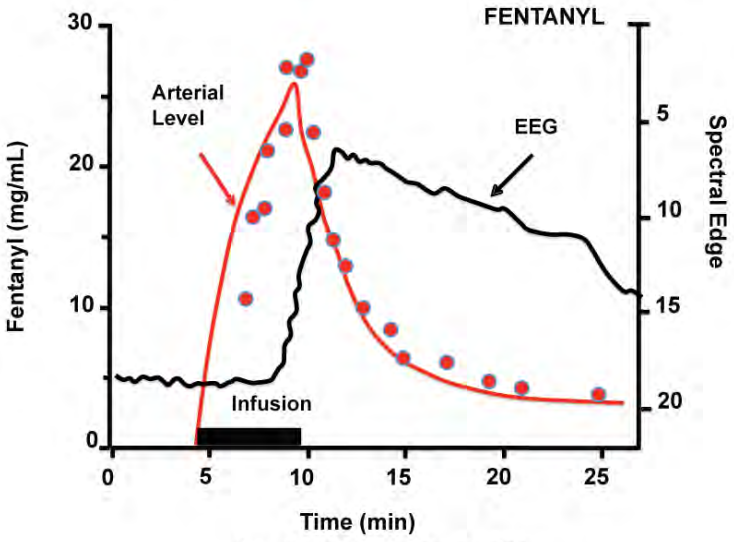
  Opioid agonists bind to specific opioid receptors (primarily Mu receptors) distributed throughout the neuraxis. Opioids inhibit spontaneous neuronal firing and excitatory neurotransmitter release. The desired clinical effects of opioids are dose dependent and include sedation and analgesia. Other clinical effects include respiratory depression and varying levels of bradycardia that are more common with the synthetic opioids like fentanyl. Opioids do not provide amnesia. As a class the distinguishing feature among opioid agonists at equal potent doses is their pharmacokinetic profile.

(1) FENTANYL

Intravenous Fentanyl:

Fentanyl is one of the most common opioid agonists used for procedural pain in children. It has a relatively high lipid solubility and relatively fast onset of

action. Fentanyl's peak effect is usually within 4-5 minutes following administration.[106] Respiratory depression is dose dependent.



Anesthesiology 1985; 62:221

In the figure above the peak EEG effects (clinical effect) trail peak serum concentrations by approximately 4-5 minutes. Consequently fentanyl should be administered approximately 4-5 minutes prior to the painful procedure. Fentanyl is highly protein bound and does not have active metabolites.

Recommended Use: Intravenous fentanyl doses of 0.5-2 mcg/kg over 1-2 minutes results in good analgesia. Repeat doses of 0.5 mcg/kg may be required during the procedure every 2-3 minutes. Fentanyl's duration of effect is typically 20-30 minutes, however it may be as prolonged as 60 minutes. Fentanyl combined with other agents like midazolam and propofol may have synergistic effects.[105]

Oral Transmucosal Fentanyl Citrate (OTFC):
Oral transmucosal fentanyl is available as a sweetened lozenge on a plastic stick of various strengths (200µg, 300µg and 400µg). The recommended dosage is 15-20 µg/kg orally. Generally there is excellent and rapid uptake of the drug from the oral mucosa although the effectiveness of a given dose varies with how much of the drug is swallowed by the patient rather than allowed to absorb transmucosally. Drug that reaches the stomach for absorption may be responsible for prolonged serum concentrations. Sedation reliably occurs within 15-30 minutes.[107] Note: Awareness may be maintained even when the patient appears asleep.

Adverse effects of this form of the drug are those commonly associated with mu opioid receptor agonists. Pruritis occurs in 44%. Nausea and vomiting occurs in approximately 15-20% of patients and is not prevented by the administration of antiemetics.[108] Respiratory depression with oxygen desaturation to less than 90% has been reported in 5% of children but usually resolves with verbal prompting.[109] Other adverse effects including chest wall and glottic rigidity are possible but much more common with the IV form of the drug.

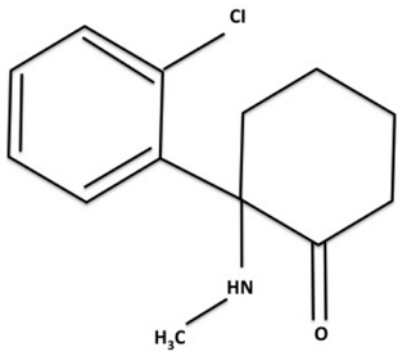
Recommended use: OTFC offers a painless method of delivering opioid, which may be of particular use in patients without an intravenous line undergoing painful procedures. Associated nausea and vomiting, and the need for more intensive monitoring and observation than other oral sedatives have limited its popularity to date. The use of pulse oximetry is mandatory in these patients even when they appear awake and alert. A medical observer must be present.

(2) MORPHINE

Intravenous morphine has stood the test of time as a main stay for controlling pediatric pain. Morphine's onset of action is slow relative to fentanyl, making it a less desirable drug for acute procedural pain. Similarly, morphine's clinical effect is prolonged, typically 2 to 4 hours. Consequently morphine is much better for postoperative pain or chronic pain management. Morphine may have some advantages for prolonged painful procedures. Below are comparisons in dosing, onset of action and duration between intravenous fentanyl and morphine.

Opioid	Dose	Repeat Dose	Onset	Duration
Morphine	0.05-0.2 mg/kg	0.05 mg/kg q 10 min	5-10 min	3-4 hours
Fentanyl	0.5-2 µg/kg	0.5 µg/kg q 2-3 min	2-3 min	30-60 min

- **KETAMINE**[110]



Ketamine is a phencyclidine derivative with dissociative sedative, analgesic and amnestic properties. Ketamine noncompetitively blocks the N-methyl-D aspartate (NMDA) receptor, part of a class of glutamate receptors mediating excitatory neurotransmission. Both sodium and calcium ion fluxes into the cell are inhibited and excitatory neurotransmission is decreased. A functional dissociation is created between the cortical and limbic systems of the brain. Ketamine has a long track record of safety as a sedative for painful procedures in children.[111]

Ketamine is one of the most versatile sedative-analgesic agents and results in a number of desired clinical effects that are dose-dependent.[112] At the lowest of doses anxiolysis and analgesia occur. Antegrade amnesia occurs at slightly higher doses and is often accompanied by perceptual changes. Higher doses result in a sedated state that is often described as "dissociative sedation". Typically spontaneous respirations and airway reflexes are maintained although may not be totally normal. Ketamine generally causes an increase in heart rate, blood pressure and cardiac output and may be particularly useful in patients with hypovolemia or hemodynamic compromise. Because of concerns of potentially increasing intracranial pressure, ketamine should be used with

caution in patients with suspected increased intracranial pressure as well as open globe injuries. Ketamine's neuropsychiatric effects include visual hallucinations that may be accompanied by emergence phenomena and agitation. Oral secretions are typically only mildly increased but may require antisialogogues. The single most severe adverse effect with ketamine sedation is laryngospasm. Ketamine is clinically effective by a number of different routes.

Oral/Rectal Ketamine: Oral and rectal doses of ketamine are 4-10 mg/kg. Onset of sedation occurs in 15-30 minutes and effects may be prolonged by the oral or rectal route lasting 3 to 4 hours. Ketamine's active metabolite norketamine predominates with oral and rectal administration typically in a ratio of norketamine to ketamine of 5 to 1 and 3 to 1 respectively.[113,114] Norketamine is approximately one-third as potent as ketamine. Following oral administration (10 mg/kg), peak effects occurred in 30 to 40 minutes in children undergoing painful cancer procedures.[115] Typically, higher doses of oral ketamine (8-10 mg/kg) are more effective as a premedication than lower doses (3-6 mg/kg).[116,117]

Intranasal Ketamine:
Intranasal is an alternative route for ketamine administration. Doses of 3-9 mg/kg have been used effectively as an anesthetic premedication.[118,119] Clinical onset is usually within 5 minutes with peak ketamine concentrations occurring in ~20 minutes.[118]

Intramuscular (IM) Ketamine:
Intramuscular ketamine reaches peak blood levels and clinical effect in five minutes after 3 to 10 mg/kg. Recovery from dissociation occurs within 15 to 30 minutes with coherence and purposeful neuromuscular activity returning in 30-120 minutes. A smaller dose of 3 mg/kg has been employed to facilitate intravenous catheter placement or acceptance of a mask for anesthesia induction, with no delay in discharge compared to control patients after 60 minutes.[120] The 100 mg/ml formulation of ketamine is preferred for IM administration in older children to minimize volume related injection site discomfort. Experience with intramuscular ketamine is extensive. Sedation is accompanied by excellent analgesia. Intramuscular administration of ketamine is an excellent means of sedating the "out of control" patient for IV placement or mildly painful procedures. Deep sedation may occur.[121]

Intravenous Ketamine:
Intravenous ketamine is typically given in doses of 0.5 to 1 mg/kg although doses of 2 mg/kg can be used. Peak concentrations occur within 1 to 2 minutes and rapid absorption by the highly perfused cerebral tissues allows almost immediate induction of clinical effects. Ketamine then slowly redistributes into the peripheral tissues; thus decreasing central nervous system levels occur and correlate with return of coherence, generally 10-15 minutes.[122,123,124] Deep levels of sedation may be achieved. Remarkably painful procedures are tolerated well following administration of ketamine because of its profound analgesic effects as well as the dissociative sedation it affords.

Intravenous ketamine is well established as a safe and efficacious agent with over 90 separate series investigating its use in over 11,000 pediatric patients.[123] Because of higher blood levels with intravenous use, ketamine administered by this route may have more problems than oral or intramuscular administration. Oral secretions may be avoided by the administration of an antisialogogue (atropine 0.01-0.02 mg/kg or glycopyrrolate 0.005 mg/kg intravenous). Although patients will continue to breath and maintain airway tone, silent pulmonary aspiration of oral contents has been reported with deep levels of sedation. Patients may continue to move during sedation and eyes may remain open. Emergence delirium is much less common in children than adults and may be prevented or treated by the administration of a small dose of a benzodiazepine or preparing the patient by discussing the clinical effects of ketamine

prior to administration. However a recent study failed to demonstrate a reduction in emergence phenomena when administered with midazolam.[125] Vomiting is not uncommon, being reported in 12 to 25% in some series.[126,127] Co-administration of ketamine with midazolam reduced the incidence of vomiting.[125] In addition, intravenous ondansetron (0.15 mg/kg) reduced the incidence of vomiting from 12% to 5% in a placebo controlled study of pediatric emergency department patients.[127] Finally in over 8,000 pediatric ketamine sedations in children admitted to the emergency department, risk factors that predicted ketamine associated airway and adverse respiratory events were high intravenous doses, children younger than 24 months of age and the co-administration of anticholinergics and benzodiazepines.[128] Ketamine dosing, onset of action and clinical duration based on route of delivery is summarized below.

	Dose	Repeat Dose	Clinical Onset	Clinical Peak	Clinical Duration
IV	0.5-1 mg/kg*	0.5 mg/kg (every 2-3 min)	< 60 sec	1-2 min	10-15 min
IM	2-4 mg/kg	2-4 mg/kg	1-2 min	2-4 min	30-60 min
IN	3-6 mg/kg	——	~ 5 min	10-20 min	45 min
Oral	6-10 mg/kg*	6-10 mg/kg	~ 10-15 min (variable)	~ 20-45 min	2-3 hours
Rectal	6-8 mg/kg**	6-8 mg/kg	~ 5-10 min (variable)	10-20 min	2-3 hours

*Midazolam 0.1 mg/kg (IV)
**Midazolam 0.2-0.3 mg/kg (oral, rectal)

Recommended use: Ketamine alone is particularly effective for procedures with moderate to severe discomfort and pain. In one series initial doses of 0.5 mg/kg followed by repeat doses of 0.25-0.5 mg/kg was effective for 97% of pediatric patients undergoing invasive emergency department procedures, 40% of procedures being fracture reductions.[129] In combination with midazolam, ketamine doses of 0.5-1.5 mg/kg was superior in efficacy and safety to an opioid-midazolam combination in children undergoing painful pediatric oncology procedures[130] and for children undergoing fracture reduction.[131] Similarly the combination of propofol and ketamine, 1 mg/kg, resulted in less restlessness during burn dressing changes compared to a propofol-fentanyl combination.[132] Finally, in a double blinded, randomized controlled comparison of propofol-fentanyl to a propofol-fentanyl-ketamine (0.5 mg/kg) combination in children receiving interventional radiology procedures, those children receiving ketamine experienced fewer oxygen desaturations and required less overall propofol.[133] Ketamine should be used cautiously if at all in individuals with intracranial hypertension, systemic hypertension or neuropsychiatric disorders and/or any child with visual or auditory disturbances.

4. REVERSAL AGENTS

- **FLUMAZENIL**

Flumazenil is a short-acting agent that reverses benzodiazepine-induced sedation. Re-sedation may occur due to its short duration of action, therefore additional doses may be

necessary. Flumazenil is not useful for reversal of barbiturate- or opioid-induced sedation.

Dosing:

(1) Dose: 0.01 mg/kg IV (max. dose 0.2 mg). If desired level of consciousness is not obtained after waiting an additional 45 seconds, give repeat dose.
(2) Repeat dose: 0.005-0.01 mg/kg IV
(3) Induction time: 1-3 min (peak effect 6-10 min)
(4) Duration of effect: Usually less than 60 minutes. Duration is related to the dose given and the benzodiazepine plasma concentrations; reversal effects of flumazenil may be shorter than the effects of the benzodiazepine.
(5) Re-sedation may occur because the duration of effect of the benzodiazepine may exceed that of flumazenil. In the event of re-sedation, repeat doses may be administered at 20-minute intervals as needed.

Precautions:

(1) Should not be given to patients who are on benzodiazepines as part of therapy for a seizure disorder.
(2) Give cautiously to patients who are on medications known to lower the seizure threshold, such as tricyclic antidepressants, theophylline, isoniazid or lithium. Use of flumazenil in these patients could precipitate a seizure.

- **NALOXONE**

Naloxone is a short-acting agent that reverses opioid-induced sedation. It competes and displaces opioids at opioid-receptor sites. Re-sedation may occur due to its short duration of action, therefore repeated doses are usually needed. Naloxone is not useful for barbiturate-, benzodiazepine- or phencyclidine-induced sedation.

Dosing:

(1) Dose: 0.01 mg/kg (IV) over 30 seconds as undiluted preparation
(2) Repeat dose: 0.01 mg/kg IV may be repeated every 2-3 minutes as needed based on response
(3) Induction time: Within 2 minutes
(4) Duration of effect: 20-60 minutes. Duration is shorter than that of most opiates, therefore repeated doses are usually needed.

Clinical Effects:

(1) Re-sedation may occur, because the duration of effect of the opiate may exceed that of naloxone. In the event of re-sedation, repeat doses may be administered.
(2) Naloxone may improve alertness but should not be substituted for an adequate period of postprocedure monitoring. Monitoring (including blood pressure) must continue until the child returns to and maintains his or her baseline level of consciousness.
(3) Naloxone may precipitate withdrawal symptoms (hypertension, sweating, agitation, irritability, shrill cry, and failure to feed) in opioid-dependent children. Use cautiously in children on opioid drips.

VI. POST-SEDATION PHASE – RECOVERY AND DISCHARGE[3,4,5]

The recovery and discharge phase is probably the most neglected and poorly studied part of the sedation process. In fact very few studies specifically evaluate the post-procedure phase. This phase is characterized by a “de-escalation” of medical care, is often the longest part of the sedation process and is a time when major adverse events can occur.

In a critical incident analysis of 60 sedated children who suffered death or permanent neurologic injury, 11 were related to premature discharge.[14] Drugs associated with prolonged recovery and adverse events are typically those with long elimination half-lives (e.g. chloral hydrate, pentobarbital). A number of studies have demonstrated adverse events during the recovery phase in children receiving chloral hydrate, particularly infants. In one study risk factors in infants included a chronological age < 2 months and post conceptional age of ~ 40 weeks.[64]

A. RECOVERY AREA AND EQUIPMENT

Recovery should take place in a well-lit area that is not too removed from the sedation site itself. The recovery area should be equipped with suction, oxygen, and equipment for positive pressure ventilation. Monitoring equipment including pulse oximetry, ECG, blood pressure, and ventilation monitoring should be available as well. A record of vital signs should be kept at regular intervals until the child is awake and interactive. The health care provider, as permitted by institutional policy, who is responsible for post sedation recovery must not have any other duties other than patient recovery. Monitoring following moderate or deep sedation must include level of consciousness, oxygen saturation, adequacy of ventilation, continuous heart rate and pain assessment.

B. DISCHARGE CRITERA

Patients should be discharged only when they have met specific criteria – this should be consistent regardless of the procedure that was performed or the drugs that were used for sedation. Monitoring prior to discharge should be time and ital function based. The Modified Aldrete score is used in a number of institutions. Below are recovery and discharge criteria used by one of the author's institutions.

PHASE I CRITERIA (Modified from Connecticut Children's Medical Center Scoring System from Pediatric Procedural Sedation and Analgesia, Eds. Krauss B. Brustowicz RM: Publishers: Lippincott Williams & Wilkins, Baltimore, Maryland. 1999.)

Vital signs (VS)
- Stable 1
- Unstable 0

Respirations (Resp)
- Normal/preprocedural level 2
- Shallow respirations/tachypnea 1
- Apnea/periodic respirations 0

Level of consciousness (LOC)
- Alert, oriented/returned to pre-procedural level 2
- Arousable, giddy, agitated, disoriented 1
- Blunted response to verbal/physical stimuli 0

Oxygen saturation
- 94 – 100% or preprocedural level 2
- 88 – 92% 1
- Less than 88% 0

Color (Peripheral)
- Pink/preprocedural color 2
- Pale/dusky 1
- Cyanotic 0

Activity
- Normal gross motor function/moves on command/preprocedural level 2
- Altered gross motor function/uncoordinated walking 1
- No to minimal spontaneous movement 0

PHASE I CRITERIA SCORE:

Greater than or equal to 8 ..... When score is greater than or equal to 8 and no category has a score of 0. → Continue onto Phase II recovery (minimum of every 15 minute vital signs for 30 min)

Less than 8 .....continue with vital signs as per Sedation Policy and Procedure

PHASE II CRITERIA: may be discharged from Phase II after a minimum of 30 min (vital signs every 15 min) and by meeting the below requirements:

1. Stable respiratory status: Each breath sounds, unlabored respiratory effort, or respiratory status at baseline.
2. Able to maintain patient airway independently: manage oral secretions and demonstrate the ability to swallow.
3. No nausea/vomiting and tolerates clear liquids without emesis.
4. Level of Awareness (LOA): Awoke and alert (able to keep eyes open and converse with parents if developmentally appropriate.
5. Activity: Good head control, sits unaided, walks with assistance (if developmentally appropriate)
6. Vital Signs: Remain stable and Phase I score is maintained.

Recent data suggest the importance of discharge criteria being time based, (e.g. patients must maintain wakefulness for ≥ 20 minutes).[3,134]

Of particular note are those children who have received long acting sedative medications.[14,15] When significant effort must be made to wake these children up post sedation (shouting or shaking) it should be noted that they will often become resedated if left alone for a period of time (riding in the car). These children are not safe for discharge. Obstruction of the airway while in a car seat has been described in children who have experienced exactly this scenario.

Similarly children who have had their sedation reversed with flumazenil or naloxone should be observed for an extended period of time (2-4 hours) due to the fact that resedation can occur as the reversal agent wears off and the sedative agent still have a therapeutic blood level.[4]

C. DISCHARGE DOCUMENTATION

At the time of discharge the status of the child should be documented and the time of discharge should be recorded. Specific instructions should be given to the family of the child instructing them what to do if the child should appear sedated or have any other medical problems in the time immediately following discharge. Post sedation instructions should be age based.

VII. ADVERSE EVENTS AND EMERGENCY STATES DURING SEDATION

In the 2006 Pediatric Sedation Research Consortium (PSRC) report of 30,037 pediatric sedation/anesthesia encounters, airway obstruction, apnea and secretions/aspiration were found to be the most common serious adverse events.[135] This next section discusses the most serious adverse events that may occur during sedation as documented by the 2006 PSRC report and defined by a recent consensus-based recommendation for standardizing sedation adverse event terminology.[136] Enhancing patient safety during sedation will be focused on in the simulation training.[13]

A. AIRWAY OBSTRUCTION (PHARYNGEAL)

Upper airway obstruction is the single most serious adverse event during moderate to deep sedation and is due to pharyngeal hypotonia. Most commonly the soft palate and epiglottis “fall back” to the posterior pharynx. Effective management of pharyngeal obstruction requires proper airway positioning, jaw thrust maneuver, bag valve mask technique, and placement of appropriate airway adjuncts (oral, nasal) when appropriate.

B. LARYNGOSPASM

Laryngospasm is an emergency observed during induction of, or emergence from sedation/anesthesia. Laryngospasm may cause partial or complete airway obstruction and is defined as glottic musculature spasm. Timely recognition and appropriate intervention with

airway maneuvers and positive pressure ventilation at 100% oxygen is essential for effective treatment. The technique of applying pressure just anterior to the mastoid process, the "laryngospasm notch", while performing a jaw thrust may be effective in relieving the laryngospasm. Deepening the level of sedation with intravenous propofol (e.g. 0.5 to 1 mg/kg) or neuromuscular blockade (e.g. succinylcholine) for a nonresponsive case may be necessary.

C. APNEA - HYPOVENTILATION

The emergent response to apnea in the setting of procedural sedation consists of rapid recognition of the problem, assessment of the etiology, and appropriate treatment. Recognition of apnea is best accomplished by constant visualization of the patient, assessing for a patent airway and adequate chest wall movement. Electronic physiologic monitors serve as a valuable adjunct, and in certain procedural situations (MRI bore, draped patient) the sedation practitioner will be completely dependent on monitors to detect apnea.

The etiology of apnea can be divided into two broad categories, central or obstructive, and the recognition and response depends on the cause. Central apnea represents the lack of respiratory effort, and onset may be abrupt or preceded by a period of progressive hypopnea. In the setting of sedation, the cause of central apnea is most commonly pharmacologic. Treatment of central apnea consists of supporting oxygenation and ventilation with a bag-mask device, and removing or reversing the cause (halting sedative administration, administering reversal agents when indicated). The patient with obstructive apnea will continue to have respiratory effort with chest wall movement, although upper airway obstruction will preclude effective ventilation, eventually resulting in hypoxia. Treatment of obstructive apnea focuses on relieving the obstruction (see treatment of airway obstruction). Supplemental oxygen alone is not sufficient treatment for either central or obstructive apnea.

The absence of ventilation precedes hypoxia, especially in the patient receiving supplemental oxygen. Thus, monitoring airflow with a pretracheal stethoscope and/or continuous sidestream $ETCO_2$ monitor enables faster response to apnea than does monitoring SpO_2 alone, sometimes by several minutes. Upper airway obstruction and abrupt onset of central apnea can be detected immediately, and recognition of and response to gradual hypoventilation with escalating CO_2 values may prevent delayed onset of central apnea.

D. ASPIRATION

Pulmonary aspiration was one of the most common serious adverse events observed in the PSRC report in 2006. Loss of protective airway reflexes during sedation is the primary cause of aspiration. Aspiration is defined as the penetration of the airway, either proximal or distal, by gastric contents or oropharyngeal secretions. In a patient with intact airway clearance mechanisms and normal gastroesophageal tone and motility this does not occur. Airway clearance relies on active processes such as swallowing, reflexive mechanisms like cough as well as the passive process of ciliary motility. Increased risk of aspiration results from attenuation of these reflexes by either acute illness like RSV pneumonia, drugs such a sedatives or narcotics, or chronic co-morbidities such as cystic fibrosis. Diminished gastrointestinal tone and motility as well as decreased tone of esophageal and cardiac sphincters can increase the risk of gastric contents passing into the oropharynx and then into the distal airway. Acute illnesses such as sepsis, pneumonia, and intraabdominal infections are well known to be associated with decreased GI motility. Concomitant use of a sedative or narcotic medication in these patients will increasingly diminish GI motility and sphincter tone. Additionally, therapeutic and diagnostic maneuvers or interventions may induce aspiration. Aggressive suctioning may stimulate a gag reflex or cause coughing, both of which may promote passage of stomach contents into the oropharynx.

The clinical sequellae of aspiration of oropharyngeal secretions and gastric contents are varied and are determined by the underlying condition of the patient, the depth of sedation and the rapidity and success of intervention. The most common and benign scenario is the young child with mental retardation/cerebral palsy who drools and during induction has aspiration of oropharyngeal secretions that one can easily clear with oropharyngeal suctioning. If the intervention is

unsuccessful then progressive aspiration of the secretions into the larynx may cause coughing and potentially laryngospasm with the need for aggressive and emergent airway support such as BVM and possibly endotracheal intubation. Consequently even a benign-appearing initial event can have emergent and life-threatening consequences. Contrast that with a young infant with gastroesophageal reflux disease who requires an MRI for FTT and becomes apneic during induction. The appropriate intervention of BVM causes introduction of air into the stomach and displaces gastric contents into the airway which may then be further propagated distally by BVM and induce laryngospasm. Enthusiastic BVM may introduce excessive air into stomach displacing gastric juices into the oropharynx.

Immediate recognition of airway secretions and/or aspiration is essential to adequate treatment. Availability of airway (e.g. bag and mask) and suction equipment is necessary to treat this adverse event. Proper airway maneuvers, suctioning and bag-mask ventilation may be required.

E. CARDIOVASCULAR INSTABILITY

Hemodynamic complications during the sedation of pediatric patients can occur due to the direct cardiovascular effects of the medications used to provide sedation/analgesia, the underlying physiology of a concurrent medical illness, changes in respiratory physiology during sedation that affect the cardiovascular system, or, most commonly, a combination of these factors. All of the commonly used sedatives and analgesic medications can cause unwanted hemodynamic effects on the pediatric patient. Although some medications, such as ketamine, fentanyl and etomidate, are considered “friendly” to the cardiovascular system they may still result in hypotension, hypertension, bradycardia, and signs of poor tissue perfusion. Some of the sedative/hypnotics cause vasodilation (propofol, morphine) or are direct myocardial depressants (barbiturates, propofol, ketamine). Use of some medications can also result in hemodynamically significant bradycardia (propofol, dexmedetomidine) when used in sufficient doses. For most of the medications used in pediatric sedation the unwanted cardiovascular side effects are dose dependent and relate to the depth of sedation. In these circumstances the use of smaller doses titrated to effect can avoid the unwanted complications.

The patients underlying cardiovascular physiology can contribute significantly to the side effects of sedative/analgesic medications. Patients in a pre-existing hypovolemic state or with an inflammatory response resulting in vasodilatation may have a profound decrease in organ perfusion as a result of the bradycardia, myocardial depression, or vasodilatation caused by deeper levels of sedation. Those with decreased myocardial function at baseline prior to sedation may not tolerate the effects of sedation and/or analgesic medications and in these situations judicious use of medications that can be titrated may be the most prudent approach.

The changes that occur in the respiratory system during sedation may also have an effect on the cardiovascular system. Although in the healthy child these cardiopulmonary interactions typically go unnoticed, in the ill child the effects can be important. Inspiratory airway obstruction resulting in more negative intrathoracic pressures will increase venous return and cardiac output in the normovolemic child. However, these pressure changes will also increase LV afterload and lead to decreased cardiac output in the child with poor LV function at baseline. In general, airway obstruction on expiration will have the opposite effect on venous return and LV afterload. The change in cardiac output during sedation may be difficult to predict and will depend on the underlying cardiac function and volume status of the child.

Prior to procedural sedation in an infant or child, it is important to consider the patient’s underlying respiratory and cardiovascular physiologic state, the important side effects of the sedation/analgesia, and the procedure being performed. Advance preparation and anticipation of cardiovascular effects will contribute to the safe administration of sedation/analgesia outside of the operating room.

REFERENCES

1. Guidelines for the elective use of conscious sedation, deep sedation, and general anesthesia in pediatric patients. Committee on Drugs. Section on anesthesiology. Pediatrics 1985,76:317-21
2. American Academy of Pediatrics, Committee on Drugs. Guidelines for monitoring and management of pediatric patients during and after sedation for diagnostic and therapeutic procedures. Pediatrics 1992;89:1110-1115
3. Coté CJ, Wilson S, Work Group on Sedation. Guidelines for monitoring and management of pediatric patients during and after sedation for diagnostic and therapeutic procedures: An update. Pediatrics 2006;118(6):2587-2601
4. American Society of Anesthesiologists. Practice Guidelines for sedation and analgesia by Non-Anesthesiologists. Anesthesiology 2002;96(4):1004-1017
5. Comprehensive Accreditation Manual for Hospitals: The Official Handbook. 2006 CAMH
6. Hillman DR, Platt PR, Eastwood PR. The upper airway during anaesthesia. BJA 2003;91(1):31-9
7. Litman RS. Upper airway collapsibility. Anesthesiology 2005;103:453-454
8. Reber A, Wetzel SG, Schnabel K, Bongartz G, Frei FJ. Effect of combined mouth closure and chin lift on upper airway dimensions during routine magnetic resonance imaging in pediatric patients sedated with propofol. Anesthesiology 1999;90:1617-23
9. Alalami AA, Ayoub CM, Baraka AS. Laryngospasm: review of different prevention and treatment modalities. Pediatric Anesthesia 2008;18:281-288
10. Roussos C, Koutsoukou A: Respiratory failure. Eur Respir J 2003;22: Suppl 47, 3s-14s.
11. Pattinson KTS. Opioids and the control of respiration. Br J Anaesth 2008;100-747-58.
12. Keats AS. The effect of drugs on respiration in man. Ann Rev Pharmacol Toxicol 1985;25:41-65
13. Coté CJ, Notterman DA, Karl HW, et al. Adverse sedation events in pediatrics: A critical incident analysis of contributing factors. Pediatrics 2000;105:805-814
14. Coté CJ, Karl HW, Notterman DA, et al. Adverse sedation events in pediatrics: analysis of medication used for sedation. Pediatrics 2000;106:633-644
15. Malviya S, Voepel-Lewis T, Tait AR. Adverse events and risk factors associated with the sedation of children by nonanesthesiologists. Anesth Analg 1997;85:1207-1213
16. Williams GD, Jones TK, Hanson KA, et al. The hemodynamic effects of propofol in children with congenital heart disease. Anesth Analg 1999;89:1411-1416
17. Williams GD, Philip BM, Chu LF, et al. Ketamine does not increase pulmonary vascular resistance in children with pulmonary hypertension undergoing sevoflurane anesthesia and spontaneous ventilation. Anesth Analg 2007;105:1578-1584
18. Tait AR, Malviya S. Anesthesia for the child with an upper respiratory tract infection: Still a dilemma? Anesth Analg 2005;100:59-65
19. Jordan AS, White DP. Pharyngeal motor control and the pathogenesis of obstructive sleep apnea. Respiratory Physiology & Neurobiology 2008;160:1-7
20. Gross JB, Bachenberg KL, Benumof JL, et al. Practice guidelines for the perioperative management of patients with obstructive sleep apnea: a report by the American Society of anesthesiologists Task Force on Perioperative management of patients with obstructive sleep apnea. Anesthesiology 2006;104:1081-1093
21. Redline S, Tishler PV, Schluchter M, et al. Risk factors for sleep-disordered breathing in children. Am J Respir Crit Care Med 1999;159:1527-1532
22. Ng DK, Chow PY, Chan CH, Kwok KL, Cheung JM, Kong FY. An update on childhood snoring. Acta Paediatrica 2006;95:1029-1035
23. University Health System Consortium. Deep procedural sedation on patients without a controlled airway – best practice recommendations. August, 2006 (www.uhc.edu)
24. Fishbaugh DF, Wilson S, Preisch JW, et al. Relationship of tonsil size on an airway blockage maneuver in children during sedation. Pediatr Dent 1997;19(4):277-281
25. Mallampati SR, Gatt SP, Gugino LD, et al. A clinical sign to predict difficult tracheal intubation: a prospective study. Can Anaesth Soc J 1985;32(4):429-434
26. Vespasiano M, et al. Propofol sedation: Intensivist's Experience with 7304 cases in a children's hospital. Pediatrics 2007; 120:e1411-1417
27. Blike GT, Christoffersen K, Cravero JP. A method for measuring system safety and latent errors associated with pediatric procedural sedation. Anesth Analg 2005;101:48-58
28. Soubani AO: Noninvasive monitoring of oxygen and carbon dioxide. Am J Emerg Med 2001;19:141-146.

29. Burton JH, et al. Does end-tidal carbon dioxide monitoring detect respiratory events prior to current sedation monitoring practices? Acad Emerg Med 2006;13:500-504
30. Lightdale JR, et al. Microstream capnography improves patient monitoring during moderate sedation: A randomized, controlled trial. Pediatrics 2006;117(6):e1170-e1178
31. Krauss B, Hess DR. Capnography for procedural sedation and analgesia in the emergency department. Ann Emerg Med 2007;50(2):172-181
32. Soto RG, et al. Capnography accurately detects apnea during monitored anesthesia care. Anesth Analg 2004;99:379-382
33. Hoffman GM, Nowakowski R, Troshynski TJ, et al. Risk reduction in pediatric procedural sedation by Application of an American Academy of Pediatrics/American Society of Anesthesiologists process model. Pediatrics 2002;109:236-243
34. Fisher DM. (Almost) Everything you learned about pharmacokinetics was (Somewhat) wrong! Anesth Analg 1996;83:901-903
35. Gepts E. Pharmacokinetic concepts for TCI anaesthesia. Anaesthesia 1998;53(1):4-12
36. Minte CF, Schnider TW. Contributions of PK/PD modeling to intravenous anesthesia. Clin Pharmacol Ther 2008;84(1):27-38
37. Kern SE, Stanski DR. Pharmacokinetics and pharmacodynamics of intravenously administered anesthetic drugs: Concepts and lessons for drug development. Clin Pharmacol & Ther 2008;84(1):153-157.
38. Weisman SJ, Bernstein B, Schechter NL. Consequences of inadequate analgesia during painful procedures in children. Arch Pediatr Adolesc Med 1998;152:147-149.
39. Zeltzer LK, Altman A, Cohen D, et al. Report of the subcommittee on the management of pain associated with procedures in children with cancer. Pediatrics 1990;86:826-831.
40. Phillips D, Watson AR, Collier J. Distress and radiological investigations of the urinary tract in children. Eur J Pediatr 1996;684-687
41. Stashinko EE, Goldberger J. Test or trauma? The voiding cystourethrogram experience of young children. Issues in Comprehensive Pediatric Nursing 1998;21:85-96
42. McMillan CO, Spahr-Schopfer IA, Sikech N, et al. Premedication of children with oral midazolam. Can J Anaesth 1992;39:545
43. Coté CJ. Sedation for the pediatric patient. Pediatr Clin North Am 1994;41:31
44. Malinovsky J-M, Populaire C, Cozian A, et al. Premedication with midazolam in children. Effect of intranasal, rectal, and oral routes on plasma midazolam concentrations. Anaesth 1995;50:351
45. Cox RG, et al. Evidence-based clinical update: Does premedication with oral midazolam lead to improved behavioural outcomes in children? Can J Anesth 2006; 53:1213-1219
46. Bozkurt P. Premedication of the pediatric patient – anesthesia for the uncooperative child. Curr Opin Anaesthesiol 2007;20:211-215.
47. Elder JS, Longenecker R. Premedication with oral midazolam for voiding cystourethrography in children: Safety and Efficacy. AJR 1995;164:1229-1232
48. Stokland E, Andreassomb S, Jacobsson B, Jodal U, Ljung B. Sedation with midazolam for voiding cystourethrography in children: a randomized double-blind study. POediatr Radiol 2003;33:247-249
49. Herd DW, McAnulty KA, Keene NA, Sommerville DE. Conscious sedation reduces distress in children undergoing voiding cystourethrography and does not interfere with the diagnosis of vesicoureteric reflux: A randomized controlled study. AJR 2006;187:1621-1626
50. Saint-Maurice C, Meistelman C, Rey E, et al. The pharmacokinetics of rectal midazolam for premedication in children. Anesthesiology 1986;65:536
51. Karl HW, Keifer AJ, Rosenberger JL, et al. Comparison of the safety and efficacy of intranasal midazolam or sufentanil for preintubation of anesthesia in pediatric patients. Anesthesiology 1992;76:109.
52. Rita L, Frank LS, Mazurek A, Rabins S. Intramuscular midazolam for pediatric preanesthetic sedation: a double blind controlled study with morphine. Anesthesiology 1985;63:528
53. Sandler ES, et al. Midazolam vs fentanyl premedication for painful procedures in children with cancer. Pediatrics 1992;89:631
54. Vinik HR, Reves JG, Greenblatt DJ, et al. The pharmacokinetics of midazolam in chronic renal failure patients. Br J Anaesth 1983;59:390
55. Wattenmaker I, Kasser JR, McGravey A. Self-administered nitrous oxide for fracture reduction in children in an emergency room setting. J Orthoped Trauma 1990;4:35
56. Babl FE, Oakley E, Seaman C, Barnett P, Sharwood LN. High-Concentrationnitrous oxide for procedural sedation in children: Adverse events and depth of sedation. Pediatrics 2008;121(3):E528-E532

57. Griffin GC, Campbell VD, Jones R. Nitrous oxide-oxygen sedation for minor surgery. JAMA 1981;245:2411
58. Henderson JM, Spence DG, Komocar LM, Bonn GE, Stenstrom RJ. Administration of nitrous oxide to pediatric patients provides analgesia for venous cannulation. Anesthesiology 1990;72:269-271
59. Zier JL, Kvam KA, Kurachek SC, Finkelstein M. Sedation with nitrous oxide compared with no sedation during catheterization for urologic imaging in children. Pediatr Radiol 2007;37:678-684.
60. Zier JL, Rivard PF, Krach LE, Wendorf HR. Effectiveness of sedation using nitrous oxide compared with enteral midazolam for botulinum toxin A injections in children. Developmental Medicine & Child Neurology 2008;50:854-858
61. Houpt MI, Slesler RB, Koenigsberg SR, et al. Assessing chloral hydrate dosing in growing children. J Dent Child 1985;52:64
62. Mallot IJ, Sly PD. Effect of chloral hydrate on arterial oxygen saturation in wheezy infants. Pediatr Pulmonol 1988;5:96-99
63. Biban P, Baraldi E, Pattennazzo A, et al. Adverse effects of chloral hydrate in two children with obstructive sleep apnea. Pediatrics 1993;92:46
64. Litman RS, Soin K, Salam A. Chloral hydrate sedation in term and preterm infants: An analysis of efficacy and complications. Anesth Analg 2010;110:739-746
65. Greenberg SB, et al. High dose chloral hydrate for sedation in children undergoing CT. J Computer Assist Tomogr 1991;15:467
66. Hollman, GA, Elderbrook MK, VanDenLangenberg B. Results of a pediatric sedation program on head MRI scan success rates and procedure duration times. Clin Ped 1995;300-305
67. Sury MRJ, Hatch DJ, Deeley T, Dicks-Mireaux CD, Chong WK. Development of a nurse-led sedation service for paediatric magnetic resonance imaging. The Lancet 1999;353:1667-1671.
68. Keengwe IN, Hegde S, Dearlove O, Wilson B, Yates RW, Sharples A. Structured sedation programme for magnetic resonance imaging examination in children. Anaesthesia 1999;54:1069-1072
69. Beebe DS, Tran P, Bragg M, Stillman A, Truwitt C, Belani KG. Reports of Investigation – Trained nurses can provide safe and effective sedation for MRI in pediatric patients. Can J Anesth 2000;47(3):205-210
70. Karian VE, Burrows PE, Zurakowski D, Connor L, Poznauskis L, Mason KP. The development of a pediatric radiology sedation program. Pediatr Radiol 2002;32:348-353
71. Gozal D, Drenger B, Levin PD, Kadari A, Yaacov G. A pediatric sedation/anesthesia program with dedicated care by anesthesiologists and nurses for procedures outside the operating room. J Pediatr 2004;145:47-52
72. Heistein LC, Ramaciotti C, Scott WA, Coursey M, Sheeran PW, Lemler MS. Chloral Hydrate sedation for pediatric echocardiography: Physiologic responses, adverse events, and risk factors. Pediatrics 2006;117(3):e434-e441.
73. Strain JD, Harvey LD, Foley LC, et al. Intravenously administered pentobarbital sodium for sedation in pediatric CT. Radiology 1986;161:105-108
74. Baxter AL, Mallory MD, Spondorfer PR, et al. Etomidate versus pentobarbital for computerized tomography sedations: report from the Pediatric Sedation Research Consortium. Pediatr Emerg Care 2007;23:690-695
75. Zgleszewski SE, Zurakowski D, Fontaine PJ, et al. Is propofol a safe alternative to pentobarbital for sedation during pediatric diagnostic CT? Radiology 2008;247(2):528-534
76. Mallory MD, Baxer AL, Kost SI, et al. Propofol vs pentobarbital for sedation of children undergoing magnetic resonance imaging: results from the Pediatric Sedation Research Consortium. Pediatr Anesth 2009;19:601-611
77. Mason KP, Sanborn P, Zurakowski D, et al. Superiority of pentobarbital versus chloral hydrate for sedation in infants during imaging. Radiology 2004;230(2):537-542
78. Warden CN, Bernard PK, Kimball TR. The efficacy and safety of oral pentobarbital sedation in pediatric echocardiography. J Am Soc Echocardiogr 2010;23:33-37
79. Manuli MA, Davies L. Rectal methohexital for sedatioin of children during imaging procedures. AJR 1993;160:577-580
80. Nishina K, Mikawa K, Shiga M, Obara H. Clonidine in paediatric anaesthesia. Paediatric Anaesthesia 1999;9:187-202
81. Bergendahl H, et al. Clonidine in paediatric anaesthesia: review of the literature and comparison with benzodiazepines for premedication. Acta Anaesthesiol Scand 2006; 50:135-143
82. Mehta UC, Patel I, Castgello FV. EEG sedation for children with autism. J Dev Behav Pediatr 2004;25:102-104

83. Hammer GB, Drover DR, Cao H, et al. The effects of dexmedetomidine on cardiac electrophysiology in children. Anesth Analg 2008;106:79-83
84. Zub D, Berkenbosch JW, Tobias JD. Preliminary experience with oral dexmedetomidine for procedural and anesthetic premedication. Pediatr Anesth 2005;15:932-938
85. Berkenbosch JW, Wankum PC, Tobias JD. Prospective evaluation of dexmedetomidine for noninvasive procedures in children. Pediatr Crit Care Med 2005;6:435-439
86. Mason KP, Zgleszewski SE, Dearden JL, et al. Dexmedetomidine for pediatric sedation for computed tomography imaging studies,. Anesth Analg 2006;103:57-62
87. Ray T, Tobias JD. Dexmedetomidine for sedation during electroencephalographic analysis in children with autism, pervasive developmental disorders and seizure disorders. J Clin Anesth 2008;20:364-368
88. Lubisch N, Roskos R, Berkenbosch JW. Dexmedetomidine for procedural sedation in children with autism and other behavior disorders. Pediatr Neurol 2009;41:88-94
89. Mason KP, O'Mahony E, Zurakowski D, et al. Effects of dexmedetomidine sedation on the EEG in children. Pediatr Anesth 2009;19:1175-1183
90. Yuen VM, Hui TW, Irwin MG, et al. A comparison of intranasal dexmedetomidine and oral midazolam for premedication in pediatric anesthesia: a double-blinded randomized controlled trial. Anesth Analg 2008;106:1715-1721
91. Herztog JH, Havidich JE. Non-anesthesiologist-provided pediatric procedural sedation: an update. Current Opinion in Anaesthesiology 2007;20:365-372
92. Liddo LD, D'Angelo A, Nguyen B, et al. Etomidate versus midazolam for procedural sedation in pediatric outpatients: A randomized controlled trial. Ann Emerg Med 2006;48:433-440
93. Schenarts CL, Burton JH, Riker RR. Adrenocortical dysfunction following etomidate induction in emergency department patients. Academic Emerg Med 2001;8(1):1-7
94. EMSC Grant Panel (writing Committee)* on Pharmacologic Agents Used in Pediatric Sedation and Analgesia in the Emergency Department. Clinical policy: Evidence-based approach to pharmacologic agents used in pediatric sedation and analgesia in the emergency department. J Ped Surg 2004;39(10):1472-1484
95. Frankville DD, Spear RM, Dyck JB. The dose of propofol required to prevent children from moving during magnetic resonance imaging. Anesthesiology 1993;79:953-958
96. Dalal PG, Murray D, Cox T, et al. Sedation and anesthesia protocols used for magnetic resonance imaging studies in infants: Provider and pharmacologic considerations. Anesth Analg 2006;103:863-868
97. Gutmann A, Pessenbacher K, Gschanes A, et al. Propofol anesthesia in spontaneously breathing children undergoing magnetic resonance imaging: comparison of two propofol emulsions. Pediatric Anesthesia 2006;16:266-274
98. Eastwood PR, Platt PR, Shepherd K. Collapsibility of the upper airway at different concentrations of propofol anesthesia. Anesthesiology 2005;103-470-477
99. Cravero JP, Beach ML, Blike GT, et al. The incidence and nature of adverse events during pediatric sedation/anesthesia with propofol for procedures outside the operating room: A report from the Pediatric Sedation Research Consortium. Anesth Analg 2009;108:795-804
100. Hertzog JH, Dalton HJ, Anderson BD, et al. Prospective evaluation of propofol anesthesia in the pediatric intensive care unit for elective oncology procedures in ambulatory and hospitalized children. Pediatrics 2000;106:742-747
101. Klein SC, Hauser GJ, Anderson BD, et al. Comparison of intermittent versus continuous infusion of propofol for elective oncology procedures in children. Pediatr Crit Care Med 2003;4:78-82
102. Barbi E, Gerarduzzi T, Marchetti F, et al. Deep sedation with propofol by nonanesthesiologists. Arch Pediatr Adolesc Med 2003;157:1097-1103
103. Hollman GA, Schultz MM, Eickhoff JC, Christenson DK. Propofol-fentanyl versus propofol alone for lumbar puncture sedation in children with acute hematologic malignancies: propofol dosing and adverse events. Pediatr Crit Care Med 2008;9:616-622
104. Vuyk J, Mertens MJ, Olofsen E. Propofol anesthesia and rational opioid selection: Determination of optimal EC sub 50 – EC sub 95 propofol-opioid concentrations that assure adequate anesthesia and a rapid return of consciousness. Anesthesiology 1997;87:1549-1562
105. Hendrickx JFA, et al. Is synergy the rule? A review of anesthetic interactions producing hypnosis and immobility. Anesth Analg 2008;107:494-506
106. Scott JC, Ponganis KV< Stanski DR. EEG quantitation of narcotic effect: The comparative pharmacodynamics of fentanyl and alfentanil. Anesthesiology 1985;62:234-241

107. Nelson PF, Streisand JB, Mulder SM, et al. Comparison of oral transmucosal fentanyl citrate and an oral solution of meperidine, diazepam and atropine for premedication in children. Anesthesiology 1989;70:616
108. Lind GH, Marcus MA, Mears SL, et al. Oral transmucosal fentanyl citrate for analgesia and sedation in the emergency department. Ann Emerg Med 1991;20:1117
109. Ashburn MA, Streisand JB. Oral transmucosal fentanyl: Help or hindrance? Drug Safety 1994;11:295
110. Reich DL, Sivay G. Ketamine: An update on the first twenty-five years of clinical experience. Can J Anaesth 1989;36:189
111. Green SM, et al. Ketamine sedation for pediatric procedures: part 2 review and implications. Ann Emerg Med 1990;19:1033
112. Krystal JH, Karper LP, Seibyl JP, et al. Subanesthetic effects of the noncompetitive NMDA antagonist, ketamine, in humans. Psychomimetric, perceptual, cognitive and neuroendocrine responses. Arch Gen Psychiatry 1994;51:199-214
113. Grant IS, et al. Pharmacokinetics and analgesic effects of I.M. and oral ketamine. Br J Anaesth 1981;53:805-809
114. Pedraz JL, et al. Pharmacokinetics of rectal ketamine in children. Br J Anaesth 1989;63:671-674
115. Tobias JD, et al. Oral ketamine premedication to alleviate the distress of invasive procedures in pediatric oncology patients. Pediatrics 1992;90:537
116. Tanaka M, Sato M, Saito A, et al. Reevaluation of rectal ketamine premedication in children. Anesthesiology 2000;93:1217-1224
117. Turhanoglu S, Kararmax A, Özyilmaz A, et al. Effects of different doses of oral ketamine for premedication of children. European J of Anaesthesiology 2003;20:56-60
118. Malinovsky JM, Servin F, Cozian A, et al. Ketamine and norketamine plasma concentrations after i.v., nasal and rectal administration in children. Br J Anaesth 1996;77:203-207
119. Diaz JH. Intranasal ketamine preinduction of paediatric outpatients. Paediatric Anaesthesia 1997;7:273-278
120. Hannallah RS, Patel RI. Low-dose intramuscular ketamine for anesthesia preinduction in young children undergoing brief outpatient procedures. Anesthesiology 1989;70:598
121. Smith JA, Santer LS. Respiratory arrest following intramuscular ketamine injection in a 4-year old child. Ann Emerg Med 1993;22:613
122. Clements JA, Nimmo WS. Pharmacokinetics and analgesic effect of ketamine in man. Fr J Anaesth 1981;53:27
123. Rice LJ. Ketamine-from “star wars” to dinosaur in 25 years? P. 345. In Stanley TH, Shafer PG(eds): Pediatric and Obstetrical Anesthesia. Kluwer Academic Publishers. Dordrecht, the Netherlands, 1995
124. Herd DW, Anderson BJ, Keene NA, et al. Investigating the pharmacodynamics of ketamine in children. Pediatric Anesthesia 2008;18:36-42
125. Wathen JE, Roback MG, Mackenzie T, et al. Does midazolam alter the clinical effects of intravenous ketamine sedation in children? A double-blind, randomized, controlled, emergency department trial. Ann Emerg Med 2000;36:579-588
126. Heinz P, Geelhoed GC, Pascoe EM. Is atropine needed with ketamine sedation? A prospective, randomised, double blind study. Emerg Med J 2006;23:206-209
127. Langston WT, Wathen JE, Roback MG, et al. Effect of ondansetron on the incidence of vomiting associated with ketamine sedation in children: A double-blind, randomized, placebo-controlled trial. Ann Emerg Med 2008;52:30-34
128. Green SM, Roback MG, Krauss B, et al. Predictors of airway and respiratory adverse events with ketamine sedation in the emergency department: an individual-patient data meta-analysis of 8,282 children. Ann Emerg Med 2009
129. Bleiberg AH, Salvaggio CA, Roy LC, et al. Low-dose ketamine. Efficacy in pediatric sedation. Ped Emerg Care 2007;23(3):158-162
130. Marx CM, Stein J, Tyler MK, et al. Ketamine-midazolam versus meperidine-midazolam for painful procedures in pediatric oncology patients. J Clin Oncol 1997;15:94-102
131. Migita RT, Klein EJ, Garrison MM. Sedation and analgesia for pediatric fracture reduction in the emergency department. Arch Pediatr Adolesc Med 2006;160:46-51
132. Tosun Z, Esmaoglu A, Coruh A. Propofol-ketamine vs propofol-fentanyl combinations for deep sedation and analgesia in pediatric patients undergoing burn dressing changes. Pediatr Anesth 2008;18:43-47
133. Erden A, Pamuk AG, Akinci SB, et al. Comparison of propofol-fentanyl with propofol-fentanyl-ketamine combination in pediatric patients undergoing interventional radiology procedures. Pediatr Anesth 2009;19:500-506

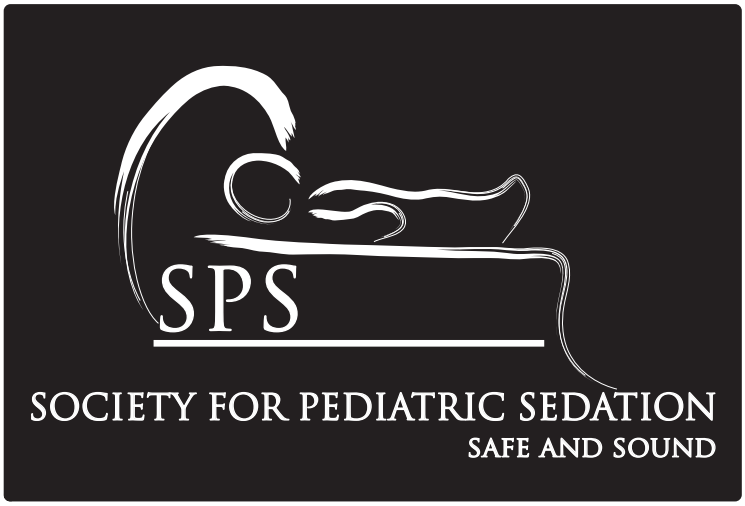
134. Malviya S, Voepel-Lewis T, Ludomirsky A et al. Can we improve the assessment of discharge readiness? A comparative study of observational and objective measures of depth of sedation in children. Anesthesiology 2004;100:218-224
135. Cravero JP, Blike GT, Beach M, Gallagher SM, Hertzog JH, Havidich JE, Gelman B, Pediatric Sedation Research Consortium. Incidence and nature of adverse events during pediatric sedation/anesthesia for procedures outside the operating room: report from the pediatric sedation research consortium. Pediatrics 2006;118(3):1087-1096
136. Bhatt M, Kennedy RM, Osmond MH, et al. Consensus-based recommendations for standardizing terminology and reporting adverse events for emergency department procedural sedation and analgesia in children. Ann Emerg Med 2009;53:426-435
137. Shavit I, Keidan I, Hoffmann Y, et al. Enhancing patient safety during pediatric sedation. Arch Pediatr Adolesc Med 2007;161(8):740-743

APPENDIX
SEDATIVE DRUGS*

Drug	Route	Dose	Repeat Dose	Onset of Action	Duration of Effect	Indication For:	Absolute & Relative Contraindications	Considerations
CHLORAL HYDRATE	Oral/ Rectal	30-100 mg/kg (may result in deep sedation) Age guidelines: 0-6 mo: 30-60 mg/kg 6-12 mo: 60-75 mg/kg >12 mo: ≥ 75 mg/kg	20 mg/kg (25-30 min after initial dose)	15-30 min	60-120 min	• Noninvasive Procedures CT ECHO MRI	• OSA • Gastritis or gastric ulcer • Hepatic dysfunction • Hemodynamic instability • Allergy to chloral hydrate • Respiratory Distress	• If repeat dose is required, assure that child is adequately alert to swallow medication. If not, administer rectally. • Monitor the child according to level of sedation. • Provide calm, quiet environment, avoiding unnecessary disturbances. • Most effective in children < 2 yo • Sedative effect less predictable with rectal administration than oral administration
CLONIDINE	Oral	3-5 mcg/kg	——	30-45 min	90 min	• Noninvasive Procedures EEG PFTs	• Hypotension • Bradycardia	• Minimal respiratory depression • Slow onset • Potential use in children with autism
DEXMEDETOMIDINE	Intravenous	1-2 mcg/kg over 10 min, Continuous infusion of 1-3 mcg/kg/hr	0.5 mcg/kg	10 min	1-2 hrs	• Noninvasive Procedures CT MRI EEG	• Allergy to Dexmedetomine • Blood pressure instability • Bradycardia • SA/AV Nodal block • Digoxin therapy	• "Cooperative Sedation" and Hypnotic effects resemble natural sleep • Less respiratory depression effects than most other sedative agents • Induction and recovery is usually very smooth. • Distinct advantage in children with Autism
	Oral Intranasal	2-4 mcg/kg 1-2 mcg/kg	——	45 min 30 min	2 hrs 90 min			
ETOMIDATE	Intravenous	0.2-0.3 mg/kg		1 min	10-15 min	• Noninvasive Procedures CT • Invasive Procedures (+) analgesic	• Airway Instability • Respiratory Distress	• Expect deep sedation immediately • Myoclonus may occur • Transient adrenocortical dysfunction
FENTANYL	Intravenous	0.5-2 mcg/kg (infused slowly over 1-2 min)	0.5-1 mcg/kg IV every 2-3 min.	2-3 min (peak effect 4-5 min)	30 min	• Invasive Procedures ± BNZ-Propofol Heme-Onc Orthopedic	• Airway instability • Cardiopulmonary compromise • Allergy to fentanyl	• Chest wall rigidity and apnea can occur with rapid administration and high doses. • Expect deep sedation. • Effects are accentuated by concurrent benzodiazepines. • Respiratory side effects may "reoccur" following completion of painful procedure. • Good opioid choice for acute, procedural pain.
	OTFC	15-20 mcg/kg		15-30 min				
KETAMINE	Intravenous	0.5-1.0 mg/kg (±) Midazolam 0.1 mg/kg IV Atropine .01-.02 mg/kg IV	0.5 mg/kg IV	1-2 minutes	10-20 min	• Invasive Procedures • Distressful Procedures	• Increased intraocular pressure • Intracranial hypertension • Intracranial mass • Hypertension • Psychiatric hx • Allergy to ketamine	• Expect deep sedation and monitor accordingly. • Ketamine can cause unusual dreams or hallucinations. Prepare the child for a floating feeling and dreaming. • The child may appear to be more alert than really is. • IV Ketamine will need to be repeated if the procedure is greater than 10-15 minutes. • Amnesia is usually obtained. • Nausea is a common side effect. • Ketamine causes nystagmus. Inform parents that this is a normal, expected effect. • Oral Ketamine has a bitter taste. Some children tolerate oral ketamine better if mixed with a small amount of juice.
	Oral Rectal	6-10 mg/kg 4-8 mg/kg (±) Midazolam 0.2 mg/kg Atropine 0.02 mg/kg		20-30 min 15-20 min	1-2 hours			
	Intranasal	3-9 mg/kg	——	5-10 min	30-45 min			

Drug	Route	Dose	Repeat Dose	Onset of Action	Duration of Effect	Indication For:	Absolute & Relative Contraindications	Considerations
METHOHEXITAL	Rectal	25-30 mg/kg	——	5-15 min	30-90 min	• Noninvasive Procedures CT	• Airway instability • Respiratory distress • Temporal lobe seizures • Cardiovascular instability • Allergy to methohexital	• Expect deep sedation and monitor accordingly • Onset of action is variable. Remain with child throughout sedation. • Dilute to 10% solution with sterile water • Airway obstruction and respiratory depression are potential side effects.
MIDAZOLAM	Intravenous	0.05-0.1 mg/kg per dose up to .2 mg/kg total dose	0.025-0.05 mg/kg	1 min	30 min	• Distressful Procedures • Premedicant • Invasive Procedures (+) analgesic	• Airway instability • Respiratory distress • Cardiovascular compromise • Allergy to midazolam	• Very good premedicant and adjunct with opioids. • Potent antegrade amnestic • Disinhibition may occur. • Children may complain of dizziness • Poor hypnotic
	Intranasal	0.2-0.4 mg/kg		10 min	60 min			
	Oral Rectal	0.3-0.75 mg/kg		15-30 min 15-20 min	60 min			
MORPHINE	Intravenous	0.05-0.2 mg/kg	0.025-0.1 mg/kg titrate every 10-15 min until desired effect	2-6 min (peak effect 10-20 min)	2-4 hrs	• Invasive Procedures (long duration) wound care	• Airway instability • Respiratory distress • Cardiovascular compromise • Allergy to morphine	• Difficult to titrate for procedural pain control. • Effects are accentuated by concurrent benzodiazepine use. • Histamine release may result in flushing and itching.
PENTOBARBITAL	Intravenous	2-6 mg/kg (usual 4 mg/kg) ~ max single dose 160 mg	1-3 mg/kg (4-5 min after initial dose)	1-2 min	45-60 min	• Noninvasive Procedures CT MRI	• Airway instability • Respiratory distress • Cardiovascular compromise • Porphyria • Allergy to barbiturates	• Expect loss of consciousness and deep sedation in minutes. • Monitor child immediately following administration and throughout sedation. • Airway obstruction and respiratory depression are potential effects. • Induction is best achieved in a quiet, dimly lit environment; keep stimulation to a minimum.
	Oral	4-5 mg/kg	2 mg/kg	10-20 min	60-100 min			
PROPOFOL	Intravenous	1-2 mg/kg per minute until asleep (total ~3-5 mg/kg) then Continuous infusion at 50-150 mcg/kg/min	0.5-1 mg/kg bolus	1 min	5-10 min	• Noninvasive Procedures • Invasive Procedures ± analgesic	• Airway instability • Respiratory distress • Cardiovascular compromise	• Expect loss of consciousness and deep sedation immediately • Potential for respiratory depression and hypoxemia is high. Preemptive O2 administration is indicated. • Potential for cardiovascular depression is high. • Peripheral administration of propofol can be painful (use with lidocaine).

*Note: Sedative dosing must take into account the nature of the patient including their level of consciousness and any coexisting illnesses. Dose ranges are approximations and some doses listed are larger than the manufacturer recommends, however doses listed are those reported in the literature to be effective.



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