

**MercyOne Siouxland Medical
Center (Sioux City, IA)**

**Adult
Moderate/Deep Sedation Study Guide**

Updated 2013

Table of Contents

| | |
|--|----|
| Introduction | 2 |
| Sedation Definition | 3 |
| Protocol Requirements | 4 |
| ASA Class..... | 5 |
| Sedation Scale..... | 5 |
| Flowchart for Sedation Guidelines..... | 6 |
| Pre-sedation Assessment..... | 7 |
| Airway Assessment | 7 |
| Risk Factors for Difficult Airway | 8 |
| Mallampati Classification | 9 |
| “At Risk” Patients | 10 |
| NPO Requirement | 10 |
| Sedation Plan | 11 |
| Documentation for Sedation | 12 |
| Consent for Sedation | 12 |
| Requirements for staff | 12 |
| Patient Care and Monitoring | 12 |
| Supplemental Oxygen | 13 |
| End Tidal CO2 Monitoring | 14 |
| Complications of procedural sedation..... | 15 |
| Airway Obstruction | 16 |
| Detecting and Treating | 16 |
| Ventilatory Techniques | 17 |
| Medications for Moderate Sedation | 18 |
| Opioids (Morphine, Hydromorphone, Meperidine, Fentanyl, Sufentanil)..... | 19 |
| Benzodiazepines (Diazepam, Midazolam, Lorazepam) | 22 |
| Combination of Opioid and Benzodiazepine | 25 |
| Reversal Agents for Moderate Sedation Medications | |
| Naloxone..... | 26 |
| Flumazenil | 28 |
| Deep Sedation Agents | |
| Propofol | 29 |
| Etomidate..... | 30 |
| Methohexital | 31 |
| Ketamine..... | 32 |
| Vasoactive Medications | 33 |
| Ephedrine | 33 |
| Phenylephrine..... | 33 |
| Atropine | 33 |
| Glycopyrrolate..... | 33 |
| Documentation Requirements | 34 |
| References | 35 |

INTRODUCTION

What Is “Procedural Sedation”?

In recent years, more and more procedures have moved from the operating room to the outpatient procedure area and patient bedside. As technology has expanded the possibility of diagnosis and treatments outside the Operating Rooms, there has been an increasing use of sedation and/or analgesia (in lieu of traditional anesthesia) to maintain patient comfort in the face of painful and/or lengthy procedures. This practice is commonly referred to as “procedural sedation”.

All physicians require appropriate skills and knowledge to safely provide sedation and analgesia to patients undergoing minor surgical and medical therapeutic or diagnostic procedures. A patient's anxiety and some degree of pain can be relieved by providing intravenous sedatives and analgesics, which have a short duration of action but unfortunately have the potential of causing **hypoxemia, acute apnea and hemodynamic instability**. Therefore, any time a patient is to receive an intravenous sedating drug prior to a procedure, it is important that the physician understands the clinical pharmacology of the medication and is able to handle the consequences of respiratory depression/arrest and hemodynamic instability.

This Study Guide is intended for non-anesthesiologists of the Medical Staff at Bakersfield Memorial Hospital and is intended only as a review of Procedural Sedation Practice. Although applicable to the pediatric patient, it is intended for use primarily in the adult population. Upon completion of this Study Guide, the physician should be aware of the requirements/protocol regarding Procedural Sedation practice as well as more general information regarding sedation scoring, pre-sedation assessment, ASA classification, airway assessment, and medications frequently administered.

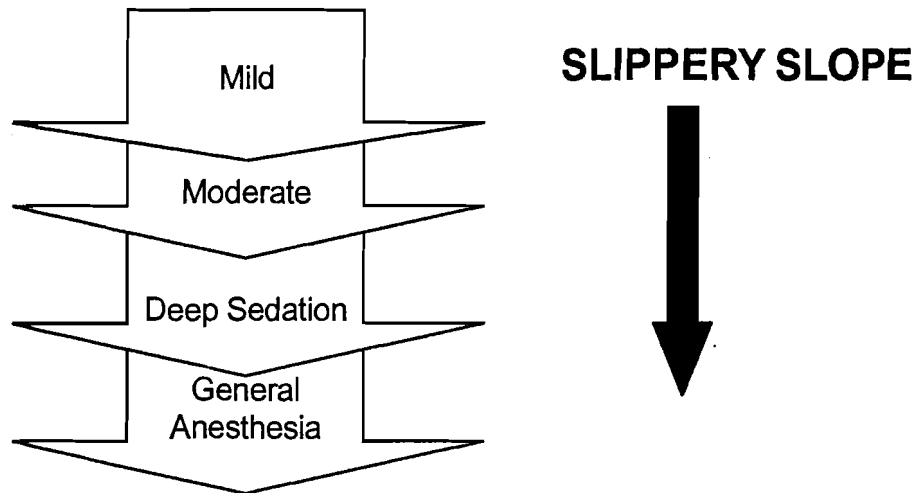
Procedural sedation refers to the following two states of drug induced depression of consciousness:

- Moderate sedation (sedation levels 2 and 3): The patient can respond to verbal or light tactile stimuli **and** maintain a patent airway without intervention
- Deep sedation (sedation level 1): The patient can respond purposefully to painful stimuli **but** may require assistance to maintain a patent airway and adequate ventilation

Note: Please refer to page 5 of this manual for an overview of the classification of Levels of Sedation.

Why All The Concern About Sedation During Procedures?

- Sedation occurs on a continuum, which is generally dose related
- This continuum also relates to the patient's ability to maintain an independent airway



REMEMBER:
A patient can proceed from mild sedation to deep sedation or general anesthesia without the intent of the physician. This is a dangerously slippery slope, which requires constant vigilance.

- It is critical to understand that procedural sedation occupies a point on the continuum between wakefulness and general anesthesia. This line is easily crossed. It is essential that anyone practicing procedural sedation be aware of the potential to sedate too deeply with unintended respiratory and hemodynamic effects.
- Patients must also be assessed and adequately prepared for the procedure in order to minimize risks.
- Constant monitoring is required to protect the patient.
- One of the requirements of The Joint Commission (TJC) is that the anesthesia standards which apply when patients receive general or major regional anesthesia also apply when they receive sedatives or analgesics, by any route, for any purpose, or in any setting, that may be reasonably expected to result in the loss of protective reflexes – (an inability to handle secretions without aspiration or to maintain a patent airway independently).
- The Procedural Sedation Guidelines/Protocol have been designed to be applicable to patients receiving sedation/analgesia for diagnostic, therapeutic, and minor surgical procedures performed in a variety of settings by practitioners who are not specialists in Anesthesiology.

The Procedural Sedation protocol includes requirements regarding the management of all patients whether receiving moderate or deep sedation.

- **Pre-sedation activities** which must be completed and documented.
 - ✓ Pre-sedation Assessment
 - ✓ Sedation Plan
 - ✓ Informed Patient Consent
 - ✓ Written orders for sedation/analgesia medications
- Patient care and monitoring requirements during and after the procedure
- Discharge criteria and Instructions
- Documentation Requirements

Note if you are planning a bedside procedure it is important that you let the nursing staff know as soon as possible of your intended schedule. This will facilitate the preparation of the patient and the availability of the staff to assist you with your procedure and ensure patient safety and comfort.

Defining the Patient:

1. All adult/pediatric patients who receive any intravenous dosage of a narcotic specifically for sedation/analgesia to facilitate a diagnostic, therapeutic, or minor surgical procedure.
2. All adult/pediatric patients who receive any COMBINATION of anxiolytic, analgesic, sedative, or hypnotic drugs for sedation/analgesia to facilitate a diagnostic, therapeutic or minor surgical procedure.
3. Excluded are patients receiving medications for pain control, seizures, pre-operative anxiety or intubated patients receiving medications while on ventilatory support.

What is an ASA Class?

- It is an **anesthesia classification code**, which helps the practitioner to identify patients who may be at risk for complications associated with sedation/analgesia. It is an attempt to classify the functional status of the patient.

| American Society of Anesthesiologists (ASA) | |
|--|--|
| ASA 1 | Healthy patient without medical problems |
| ASA 2 | Mild systemic disease or conditions controlled on treatment (eg: diabetes mellitus; smoking; asthma; thyroid disease; anemia; chronic bronchitis) |
| ASA 3 | Severe systemic diseases that limit activity but are not incapacitating (eg: complicated or uncontrolled diabetes mellitus; uncontrolled hypertension; coronary artery disease; COPD; CVA; symptomatic asthma under treatment; sleep apnea; extreme obesity—BMI greater than 40) |
| ASA 4 | Severe life threatening systemic disease (eg: severe CAD; CHF; ESRD; steroid dependent COPD; oxygen dependent COPD; persistent angina) |
| ASA 5 | A moribund patient not expected to survive with or without intervention. |
| ASA E | Emergent status—added if any of the above categories is an emergency |

What is a Sedation Scale?

Level of Sedation Scale:

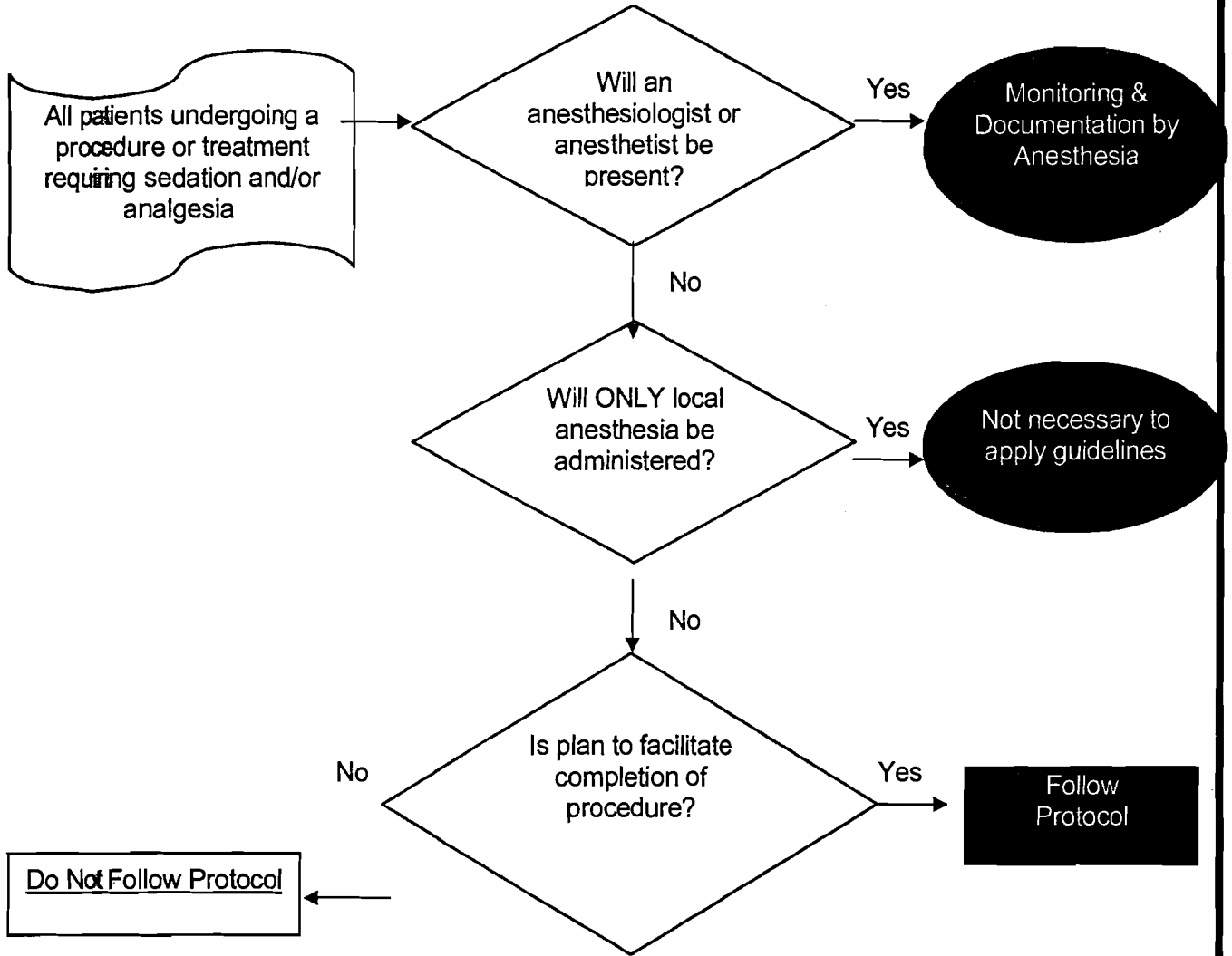
**Procedural
sedation**



| | |
|---|---|
| 0 | General Anesthesia: no purposeful response to stimuli |
| 1 | Deep sedation: purposefully responds to noxious stimuli |
| 2 | Moderate sedation: purposefully responds to verbal stimuli or light tactile stimuli |
| 3 | Moderate sedation: intermittent awareness, easily aroused by verbal stimuli |
| 4 | Minimal sedation: drowsy, conversant |
| 5 | Minimal sedation: awake, alert (baseline level of consciousness) |

- The Level of Sedation Scale is used throughout **the facility** in order for physicians, nurses and other patient care personnel to easily and consistently assess the patients' sedation level.
- It is used to describe both the **intended** level of sedation and **actual** level of sedation.

When Do Sedation Guidelines Need to be Applied?



NOTE: exclude mechanically ventilated ICU patients

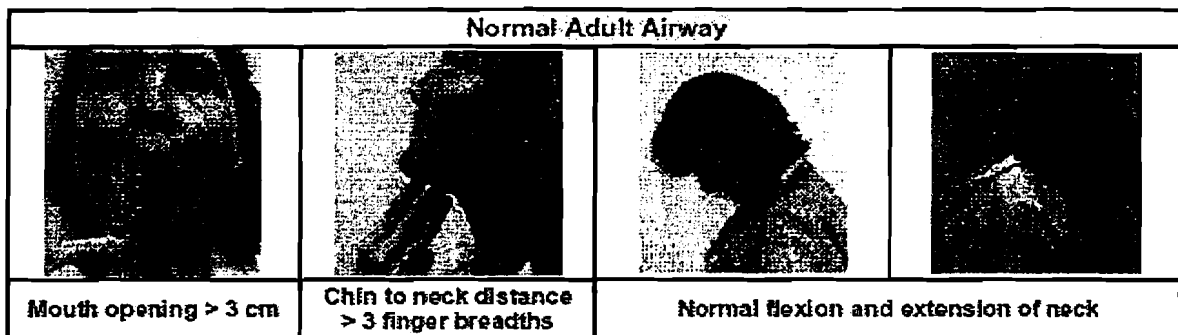
The Pre-sedation Assessment

The pre-sedation assessment includes the following:

- A current H & P
- Review of current medication history
- Allergies
- **Airway assessment**
- ASA Classification
- NPO Status
- Vital signs
- Baseline oxygen saturation

Why the Airway Assessment?

- It is critical to assess the patient's airway for ease of intubation in the event that the patient will require intubation. If the patient proves to have abnormalities, it may be prudent to request an Anesthesiology consult prior to the procedure. This is especially recommended for patients who are at high risk for loss of respiratory and protective reflexes.



Airway Assessment:

The patient should be questioned about symptoms suggestive of airway abnormalities, such as shortness of breath or hoarseness. Information should also be sought regarding previous surgery, trauma or neoplasia involving the airway and prior anesthetic experiences.

The head should be viewed in profile to detect a small or receding jaw and or the presence of protruding teeth. Loose, capped and prosthetic teeth should be noted.

Note: it can be difficult to secure a tight seal with a face mask in edentulous patients and in patients with facial hair.

Temporomandibular joint mobility is assessed by asking the patient to open the mouth. In the adult, the distance between the upper and lower central incisors is normally 4-6 cm. Ankylosis of the temporomandibular joints is seen most frequently in patients with rheumatoid arthritis. It is also prevalent in patients with Type I diabetes mellitus. In trauma patients or those who have an infection involving the mouth or neck, mobility may be restricted by pain.

The normal range of flexion-extension of the neck varies from 90-165 degrees. **Any type of neck movement that produces paresthesias or sensory or motor deficits must be documented and avoided.**

Note: The **five risk factors** that are most consistently associated with a difficult airway are:

- **Protruding maxillary incisors (buck teeth)**
- **Receding mandible**
- **Reduced jaw movement**
- **Decreased head and neck movement**
- **Obesity**

What is the Mallampati Classification?

- The Mallampati is a classification code for airway assessment and attempts to predict if a patient will be difficult to intubate. As the class increases from Class I to Class IV, the potential for difficult intubation increases.
- In order to view the uvula, tonsillar pillars and soft palate ask the seated patient to “open your mouth and stick out your tongue”

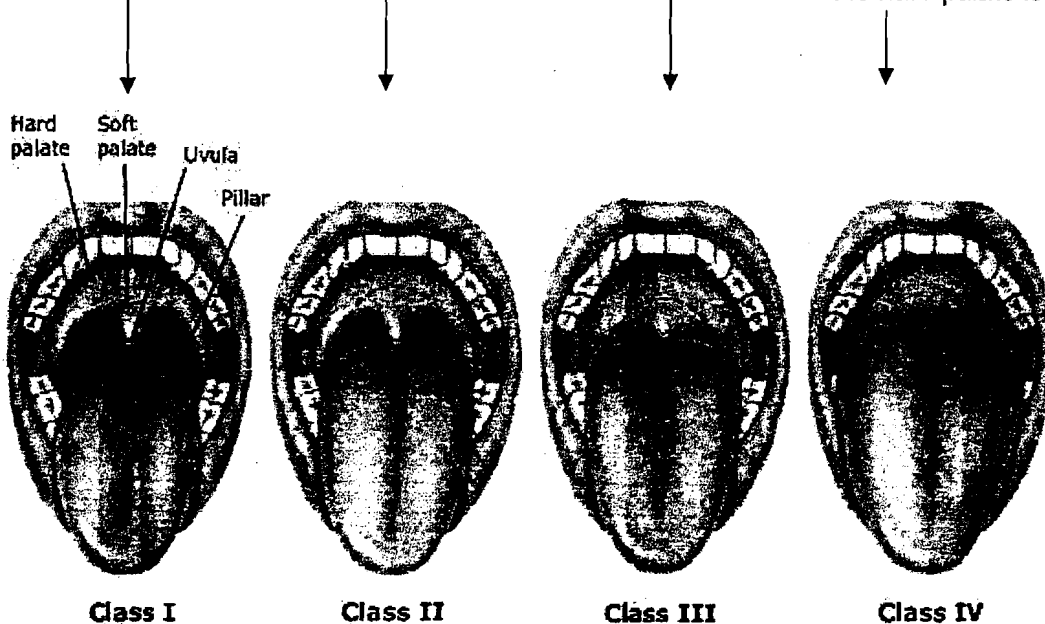
According to the Mallampati classification:

class one is present when the soft palate, uvula, and pillars are visible

class two is present when the soft palate and uvula are visible

class three is present when the soft palate and only the base of the uvula are visible

class four is present when only the hard palate is visible



- A difficult intubation may be predicted by the inability to visualize certain pharyngeal structures (class III or IV) during examination of the seated patient.
- Patients who are at risk for loss of airway and have a **Class IV** Mallampati should be considered for difficult airway evaluation by the staff of the Department of Anesthesiology prior to sedation.

Patients at high risk of complications:

- Patient has underlying health conditions that could be exacerbated by sedative medications.

For example:

1. neurological impairment
 2. concurrent hypotension, hypovolemia
 3. recent myocardial infarction
 4. adrenal insufficiency
 5. long term steroid use
 6. severe COPD
 7. sleep apnea
 8. obvious anatomical airway abnormalities
 9. pregnancy
- Patient has not maintained NPO status
 - Patient has received prior sedation/analgesic medications within previous 12 hours
 - Patient has received a monoamine oxidase (MAO) inhibitor within last 14 days—any questions regarding medications call pharmacy

What is the NPO Requirement?

- In order to minimize the danger of aspiration during the procedure, patients should not drink fluids or eat solid foods for the period of time as outlined

| NPO Guidelines | |
|---|--|
| Adult Patients | NPO for solids, milk, pureed or tube feeding x 8 hours NPO for clear liquids x 3 hours |
| Pediatric Patients | 0-2 years: NPO for breast milk, clear liquids x 4 hours NPO for formula or solids x 8 hours |
| EXCEPTION: Physician must document the emergent (ASA class E) nature of the procedure requiring administration of sedation to a patient not meeting NPO guidelines | |

.Clear liquids are: (ie: water, apple juice, grape, cranberry, Gatorade, pulp-free popsicles, Pedialyte, Koolaid and plain Jello.)

What If the NPO Requirement Can't Be Met?

- Consider the risk of aspiration versus the risk of delaying the procedure until NPO requirements are met. If the procedure is emergent, consultation with an anesthesiologist should be considered.

Sedation Plan

The Sedation Plan ensures the safety and comfort of your patient. In order to develop a plan to maximize patient safety and comfort, the information discussed below should be considered.

- The amount of discomfort or pain typically experienced during this type of procedure
- The individual patients' ability to handle the discomfort and stress of the procedure both physically and psychologically
- The patient's wishes regarding sedation.
- The pharmacodynamics and kinetics of the medications.

The following information should be incorporated into the plan:

- The specific procedure
- The individual patient
- Medications to be administered

| Procedure Variables | Patient Variables | Drug Variables |
|---|--|---|
| <ul style="list-style-type: none">• Typical experience of pain or discomfort• Duration of Procedure• Need for immobilization• Need for patient participation | <ul style="list-style-type: none">• Age• Obesity• Sleep apnea• Liver and Kidney function• Cardio-Respiratory function• Ability to cooperate or communicate• Ability to handle anxiety and/or pain• Known allergies and past reactions | <ul style="list-style-type: none">• Desired properties• Metabolism• Rate of Clearance• Rapidity of onset• Adverse effects |

Documentation of the Plan

- The physician performing the procedure and knowledgeable about the risks/benefits of the procedure and sedation/analgesia shall obtain and document informed consent.
- Except in emergency situations, either the patient or legally responsible individual must give this consent.

Patient Care and Monitoring Requirements

- **Equipment and supplies:**

The most common complication associated with procedural sedation is respiratory. One must always be prepared and anticipate for the provision of respiratory support. Therefore, equipment and supplies that must be readily available include:

- Standardized crash cart with full oxygen tank
- Supplemental wall oxygen
- Emergency airway equipment, appropriately sized for patient
- Suction equipment
- Pulse oximetry monitor
- ECG monitor
- Non-invasive blood pressure monitor
- CO₂ (end tidal or transcutaneous) monitor
- Appropriate pharmacologic agents and antagonists (reversal agents)
- Sufficient personnel to perform the procedure and monitor the patient. The person performing the procedure cannot also monitor the patient.
- Working telephone or means of two-way communication in the room

Moderate Sedation requires: Licensed Independent Practitioner (Physician) and Qualified RN

Deep Sedation requires: Physician; Qualified RN and Respiratory Therapist (to manage the airway)

Minimal monitoring required includes (the following parameters are continuously monitored):

- Level of sedation
- Pulse rate
- Respiratory rate
- Oxygen saturation
- Blood Pressure
- ECG
- End-tidal CO₂

Note: These parameters are documented prior to sedation and within 5 minutes of initial and incremental medication administration, and at least every 5 minutes during the procedure until return to baseline. Post-procedure, monitor every 6 minutes until the patient meets discharge criteria.

Supplemental Oxygen

The use of supplemental oxygen during sedation may have unintended consequences as it diminishes the value of pulse oximetry as a monitor of adequate ventilation. In the presence of supplemental oxygen, hypoventilation may lead to dangerously high levels of carbon dioxide before hypoxemia becomes apparent.

Supplemental oxygen may also cause apnea in patients who are dependent on central respiratory drive alone. Such diagnoses include:

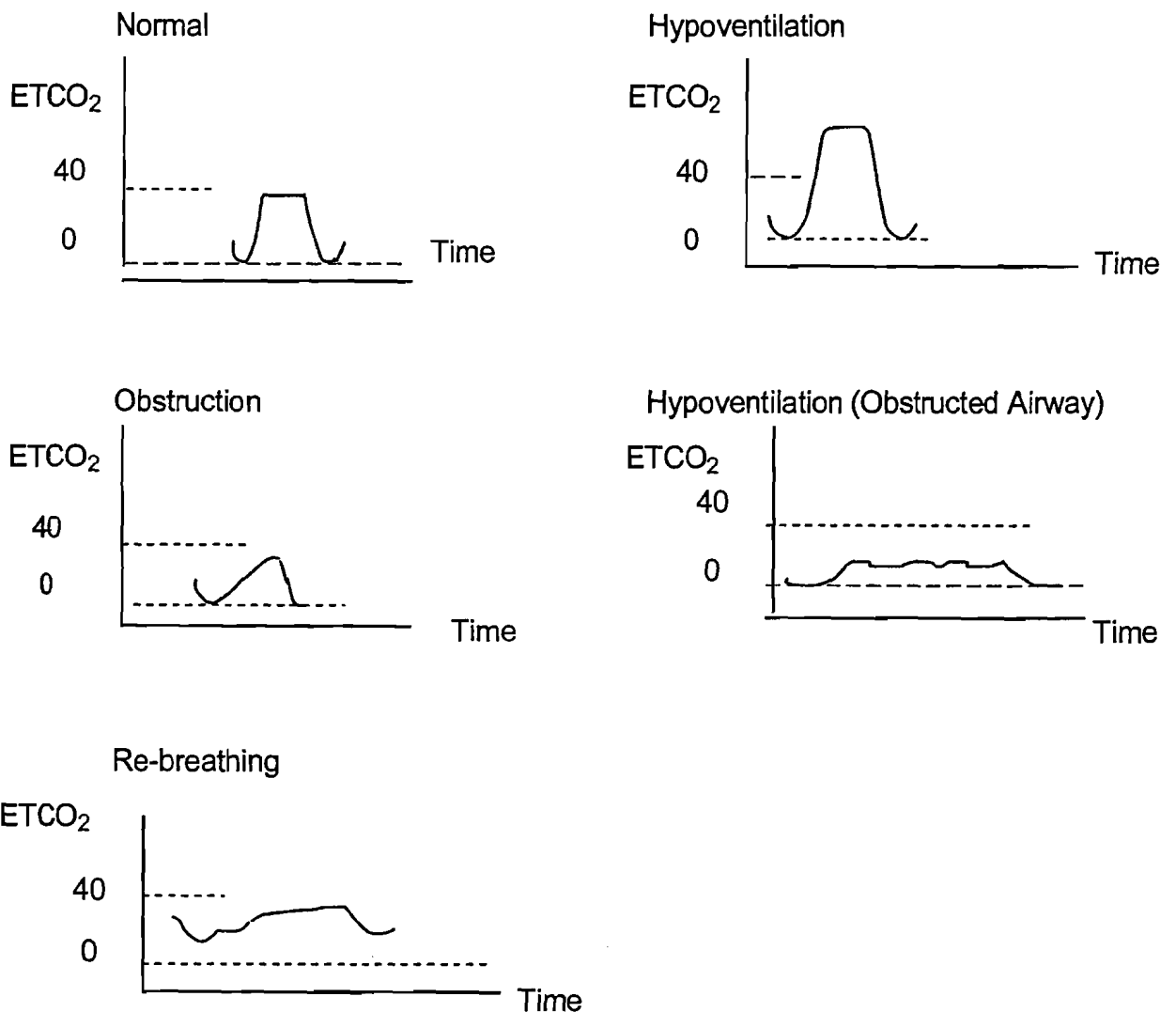
- Chronic CO₂ retention
- Post bilateral carotid endarterectomy
- Use of antidopaminergic drugs (eg: phenothiazines)
- Severe sleep apnea

End-Tidal CO₂ monitoring

End-tidal CO₂ monitors used in conjunction with nasal cannulae afford only a qualitative measure of actual end-tidal CO₂ levels. A correlation between the respiratory pattern and end-tidal CO₂ should be established before sedation is initiated. The cannulae may be placed in either the nose or mouth depending on the patient's mode of breathing.

The waveform should be examined for height, frequency, rhythm, baseline, and shape. Height depends on the concentration of carbon dioxide (in the presence of an unobstructed airway). Airway obstruction masks the extent of hypoventilation. Frequency depends on respiratory rate. Rhythm depends on the state of the respiratory center. The baseline should be zero unless carbon dioxide has been deliberately added to inspired gases.

The capnograph should demonstrate a sharp increase in CO₂ with the onset of exhalation, a plateau representing alveolar gas and a steep descent to baseline as the following inspiration begins.



Patient Care for Procedural Sedation:

All components of the Guidelines/Protocol must be followed and documentation completed. A qualified individual (usually a nurse) will be available to:

- Initiate the pre-sedation assessment
- Assist with obtaining patient consent
- Have all equipment and supplies ready
- Administer the ordered medications (**Note: Physician must administer deep sedation agents**)
- Provide continuous monitoring of the patient before, during and after the procedure
- Document required information in the medical record (Procedure Monitoring Form)
- Discharge the patient from the procedure area after the recovery period is completed

Complications of Procedural Sedation:

Adverse reactions to procedural sedation medications may cause any or all of the following. The need for appropriate intervention should be anticipated. The most common reactions include:

- Airway obstruction
- Hypoxemia
- Hypercapnia
- Loss of airway reflexes
- Aspiration of gastric contents
- Nausea, vomiting
- Hypotension
- Arrhythmias
- Anaphylaxis

Physiologic parameters/changes requiring intervention and documentation:

- a. Baseline oxygen saturation of less than 93%, a decrease in oxygen saturation from low saturation baseline, or a fall in oxygen saturation of 5% or greater.
- b. Inadequate ventilation and/or **inability to maintain a patent airway.**
- c. Inability to respond appropriately to physical stimulation/verbal commands
- d. Hemodynamic instability, as evidenced by hypotension, arrhythmia, chest pain, etc.
- e. Other adverse reactions to drugs administered.

Interventions should include:

- a. Give supplemental oxygen
- b. If saturation does not improve:
 1. Stimulate the patient.
 2. Halt procedure.
 3. Attempt to improve the airway with jaw thrust and/or oral/nasopharyngeal airway.
 4. Initiate or assist ventilation with bag/valve/mask and oxygen.
 5. Administer naloxone and/or flumazenil as appropriate.
 6. Initiate cardiopulmonary resuscitation procedures as needed.
- c. If endotracheal intubation is required, determine correct tube placement by carbon dioxide detection, presence of equal breath sounds and presence of chest rise. When appropriate, tube position should be verified by x-ray.

Detecting Airway Obstruction:

The most frequent site for airway obstruction is the oropharynx. With sedation, there is relaxation of the jaw and tongue such that the base of the tongue may fall back in contact with the posterior pharynx. If obstruction occurs the oropharynx should be examined to ensure that the obstruction is not from a foreign body.

Airway obstruction can also be caused by reflex closure of the vocal cords or laryngospasm. This typically occurs during sedation when the larynx is irritated by contact with secretions, or when the patient experiences a painful stimulus. Partial laryngospasm is characterized by high pitched phonation or "crowing". Total occlusion is characterized by no sounds but signs of airway obstruction such as retraction of the trachea or flaring of the nostrils.

Other signs of airway obstruction include: decreased or absent breath sounds; decreased or absent ETCO₂; paradoxical respiratory pattern; and decreased oxygen saturation.

Note: decreased oxygen saturation is a late feature of hypoventilation.

Treating Airway Obstruction:

The clinician should place his or her hands behind the angle of the patient's mandible and move it forward, taking care to avoid putting pressure on the anterior structures of the neck, which can accentuate the obstruction. Other measures useful in opening the upper airway include slight extension of the neck, turning the head to the side, application of positive airway pressure to "distend" the soft tissue and insertion of an oral or nasal airway.

Depending on the cause of the obstruction, treatment should include suctioning foreign material from the oropharynx, removing any painful stimulus, administering 100% oxygen, applying positive pressure to the airway, and placing the fingers behind the angles of the mandible to maintain forward thrust. If these measures do not resolve the obstruction quickly, intubation may be required.

If gastric contents are found in the pharynx, it must be assumed that aspiration has occurred. Although aspiration may be asymptomatic at the onset, it can cause **laryngospasm**, **bronchospasm** and **severe hypoxemia**. The procedure should be terminated as quickly as possible and the patient admitted for appropriate observation and treatment.

Ventilatory Support:

The ability to assist with respirations with a bag-valve device and mask is a necessary skill for those providing procedure-related sedation. The use of the bag-valve device and mask has several advantages: it provides an immediate means of ventilatory support; conveys a sense of compliance of the patient's lungs to the rescuer; can be used with spontaneously breathing patients; and can deliver an oxygen-enriched mixture to the patient.

The most frequent problem with the bag-valve-mask device is the inability to provide adequate ventilatory volumes to a patient who is not endotracheally intubated. This most commonly results from the difficulty of providing a leak-proof seal to the face while maintaining an open airway. It also occurs when the bag is not squeezed sufficiently enough to force an adequate amount of air into the patient's lungs.

The following points are offered as a review of effective ventilation techniques:

1. A bag-valve mask device used in emergency situations should not contain a "popoff" valve. The pressure required for ventilation in many situations may exceed the pop-off limit and delivered tidal volume may be insufficient.
2. Mask fit is much more important than resuscitation bag size to ensure adequate ventilation. The upper end of the mask should fit over the bridge of the nose and be well below the eyes. The lower end should be on or directly above the mandible.
3. The chin of the patient should be held forward in a sniffing position. Place the fingers of the left hand just under the mandible to support it in an anterior position (pull the face into the mask). Do not apply pressure to the soft parts of the chin, or the tongue may be pushed into the posterior pharynx and obstruct the airway further. Apply pressure to the mask primarily with the thumb and forefinger of the left hand. Chest rise must be visualized with each delivered ventilation.
4. The most advantageous position of ventilation will be slightly different for each patient. The head should be moved into various positions by flexion, extension and lateral rotation until the best airway is obtained.
5. It may be helpful to insert an oral or nasal airway.
6. To effectively use the bag-valve-mask device, the rescuer must be positioned at the top of the patient's head. Otherwise it may be impossible to maintain an effective seal between the mask and the patient's face and keep the airway open at the same time.
7. Leaks around the mask occur if the breathing bag collapses without inflating the patient's chest. To prevent leaking, change the mask position or size, or hold it more tightly in place. Do not press down on the mask and force the mandible backward—this occludes the airway. A great deal of resistance (noted by a bag that is hard to squeeze) is indicative of upper airway or lower airway obstruction. The most likely culprit is a tongue that has fallen back against the oropharynx. To correct this problem, unless trauma is suspected, further hyperextend the patient's head by applying more pressure behind the mandible with the two or three fingers of the right hand. Insert an oropharyngeal airway if the patient lacks a gag reflex. Consider foreign body obstruction, laryngospasm, tension pneumothorax and severe bronchospasm as other possible causes of airway obstruction.
8. If the head is malpositioned, gastric distension will occur as the bag is squeezed. Gastric distention interferes with ventilation by elevating the diaphragm and decreasing lung volume. Attempts at relieving gastric distention by pressure on the abdomen should be avoided because of the high risk of aspirating gastric contents into the lungs during the maneuver.
9. Allow the patient to completely exhale after each delivered breath.
10. If assisted ventilation is necessary for an extended period of time or the bag-valve-mask system fails to adequately ventilate the patient, an endotracheal tube should be inserted.

NOTE: The best indicator of effective ventilation is the rise and fall of the patient's chest.

MEDICATIONS

Overview of Medications Used During Procedural Sedation

Moderate sedation

Agents used for moderate sedation are:

Opioids:

- Morphine
- Hydromorphone (Dilaudid)
- Meperidine (Demerol)
- Fentanyl (Sublimaze)
- Sufentanil (Sufenta)

Benzodiazepines

- Diazepam (Valium)
- Midazolam (Versed)
- Lorazepam (Ativan)

Reversal agents for narcotics and benzodiazepines:

- Naloxone (Narcan)
- Flumazenil (Romazicon)

Barbiturates (oral and rectal)

- Phenobarbital

Deep sedation

These agents are used to induce deep sedation or general anesthesia and physician presence is required at the bedside prior to and during administration. **The physician must administer deep sedation agent.**

Agents used for deep sedation are:

- Propofol (Diprivan, various)
- Etomidate (Amidate)
- Barbiturates (parenteral)
- Ketamine

There are NO reversal agents for deep sedation medications. (However, patients treated with therapy that includes a deep sedation agent in combination with an opioid and/or benzodiazepine may benefit from the appropriate reversal agent).

Opioids (Narcotics)

Morphine, Hydromorphone (Dilaudid®) Meperidine (Demerol®) Fentanyl (Sublimaze®) and Sufentanil (Sufenta®)

Mechanism of Action and Adverse Effects:

- Opioids act by binding to opioid receptors primarily located in the brain and spinal cord to mimic the action of endorphins and reduce neurotransmission. The end result is activation of pain-modulating (suppression) systems.
- Opioids can also produce sedation, euphoria, dysphoria, and alterations of mood and perception of ones' surroundings.
- Adverse effects of opioids include:
 - Respiratory depression (risk increases with dose, rate of administration and concurrent administration of other respiratory depressant drugs)
 - Hypotension
 - Bradycardia (fentanyl and morphine)
 - Tachycardia (meperidine)
 - Nausea, vomiting, constipation, increased pressure in the biliary tract and spasm of the sphincter of Oddi
 - Urinary retention
 - Dizziness, mental clouding, agitation/restlessness, visual disturbances
 - Pruritus
 - Miosis (constriction of the pupils)
 - Allergic reactions (rare with fentanyl)
 - Chest wall rigidity (can occur with rapid injection of opioids, especially fentanyl)

The Differences Between Morphine, Hydromorphone, Meperidine, Fentanyl and Sufentanil:

The differences between these agents can be attributed to their affinity for opioid receptors, lipid solubility, half-life, and presence or absence of an active metabolite.

- Fentanyl and sufentanil are more potent and have a more rapid onset and shorter duration of action than morphine, hydromorphone or meperidine.
- The short duration of action of fentanyl and its derivatives results from redistribution from the CNS (its site of action) to inactive tissues (fat and muscle).
- Repeated administration or large doses of fentanyl can accumulate in fat and muscle. When accumulation occurs, the decrease in plasma concentration (which is responsible for offset of effect) is now due to elimination by the liver rather than redistribution. Therefore, the therapeutic (analgesia) and adverse (respiratory depression) effects are prolonged when repeated or large doses are administered.

Note: The respiratory depressant effects of fentanyl have a duration of action that is approximately two times longer than the analgesia.

- Sufentanil causes less hemodynamic instability, respiratory depression and chest wall rigidity than fentanyl.

| Drug | Potency ^A | Onset/ Peak Effect ^B | Duration ^B |
|---------------|-------------------------------------|--------------------------------------|-----------------------|
| Morphine | | Onset: 2-10 min. Peak: 15-30 min. | 2-6 hours |
| Hydromorphone | 5-8 times more potent than morphine | Onset: 2-10 min. Peak: 15-30 min. | 1-5 hours |
| Meperidine | 1/10 as potent as morphine | Onset: 1-10 min. Peak: 10-15 min. | 2-4 hours |
| Fentanyl | 100 times more potent than morphine | Onset: 0.5-2 min. Peak: 3-15 min. | 0.5-2 hours |
| Sufentanil | 1,000 more potent than morphine | Onset: 0.5-2 min. Peak: 3-15 min. | 0.5-2 hours |

^A 10 mg morphine = 100mg meperidine = 3 mg hydromorphone = 0.1 mg (or 100mcg) fentanyl = 0.01 mg (or 10 mcg) sufentanil

^B IV Administration

- All are metabolized in the liver.
- Reduce the dose in patients with liver dysfunction.
- Fentanyl and hydromorphone are metabolized to inactive metabolites, making them appropriate for patients with renal disease.
- Morphine and meperidine have active metabolites that are renally excreted, prolonging sedation in patients with renal compromise.

Adverse Effects of Meperidine:

- Use of meperidine in patients with either liver or renal compromise or use of large doses at short intervals causes accumulation of normeperidine, which can cause myoclonic movements, dilated pupils, hyperactive reflexes, and seizures.
 - Even in young patients with normal renal function, meperidine can cause seizures. **Do not** use on a chronic basis.
 - Daily doses of 400-600mg can result in accumulation of normeperidine.
 - CNS stimulation by normeperidine is **not** reversed by naloxone. In fact, naloxone may worsen seizures. Treat supportively with benzodiazepines or barbiturates.
 - **Do not use** meperidine in patients with underlying seizure disorders, increased intracranial pressure, sickle cell disease, hepatic or renal disease or patients taking SSRIs or MAO inhibitors.
 - MAO inhibitors, when combined with meperidine, can cause dangerous reactions such as hypertension, hyperthermia, seizures and death. **Do not administer meperidine to patients currently on MAO inhibitors or those who have taken MAO inhibitors within the last two weeks.** MAO inhibitors are phenelzine (Nardil), tranylcypromine (Parnate) and isocarboxazid (Marplan). Meperidine may also cause these effects in patients taking MAO-B inhibitors for Parkinson's disease, that is selegiline (Eldepryl) rasagiline (Azilect). For similar reasons, use of meperidine should be avoided in patients taking sibutramine (Meridia).

Note: The addition of hydroxyzine (Vistaril®) or promethazine (Phenergan®) to meperidine does **not** provide additional analgesia but **does** increase the risk of adverse effects. Respiratory depression, mental status depression and hypotension occur more frequently and phenothiazines (e.g. promethazine) lower the seizure threshold, possibly increasing the risk of normeperidine-induced CNS toxicity.

The Drug Interactions And Precautions With Opioids:

- Benzodiazepines, phenothiazines, tricyclic antidepressants and CNS depressants may be additive with or potentiate the therapeutic (analgesic) and adverse (respiratory depression) effects of opioids. **Reduce the dose.**
- MAO inhibitors as above
- Cytochrome inducers such as carbamazepine, phenobarbital, phenytoin and primidone may **increase** metabolism of fentanyl and meperidine necessitating an **increase** in opioid dose.

Special Considerations For Elderly Or Pediatric Patients:

- **Reduce the dose in elderly patients.**
 - Elderly patients are usually more sensitive to the effects of opioids.
 - Age-related changes result in decreased renal and hepatic elimination and increased volume of distribution for lipid-soluble drugs. This generally results in a longer duration of action of opioids in elderly patients.
- Altered pharmacokinetics and maturation of the blood-brain barrier may alter disposition of opioids in very young children. Use opioids with caution in infants under 6 months of age.

Benzodiazepines

Diazepam (Valium®), Midazolam (Versed®), Lorazepam (Ativan®), Alprazolam (Xanax®)

Mechanism of Action and Adverse Effects:

- Benzodiazepines occupy a receptor that modulates GABA, the major inhibitory neurotransmitter in the brain.
- Diazepam, midazolam, and lorazepam produce sedation, anxiolysis and amnesia. They also have anticonvulsant and skeletal muscle relaxant effects.
- Alprazolam is only available as a tablet. Alprazolam effectively treats anxiety and panic disorders, making it useful for sedation and anxiolysis during select radiologic procedures.
- Adverse effects of benzodiazepines include:
 - Respiratory depression
 - dose-dependent decreases in ventilation and tidal volume:
midazolam > lorazepam, diazepam
 - apnea is more likely with rapid IV administration of midazolam
 - Hypotension and tachycardia, especially in elderly, severely ill patients or in patients with an unstable cardiovascular status
 - hypotension: **midazolam** > diazepam or lorazepam

The Differences Between Diazepam, Midazolam And Lorazepam:

The differences between these agents can be attributed to their affinity for benzodiazepine receptors, lipid solubility, half-life, and the presence or absence of an active metabolite. Lipid solubility, for example, determines the drugs' ability to cross the blood-brain barrier thereby determining its potency, onset, and duration of effect. All are metabolized by the liver; however, there are differences with respect to active metabolites and variability in metabolism.

- Midazolam has a short duration of action due to rapid clearance from the CNS. Most patients clear midazolam rapidly; however, there are up to **11-fold differences** in clearance and some patients have a markedly prolonged duration of effect from midazolam.
- Diazepam has a short duration of action due to rapid clearance from the CNS. **However**, diazepam is metabolized in part to desmethyldiazepam (DMDZ), which has a half-life of **100 hours**. If metabolism of DMDZ is impaired (e.g. in the elderly) diazepam has a prolonged duration. Enterohepatic or enterogastric recirculation of diazepam may contribute to its long duration of activity.
- Ability to produce amnesia: lorazepam > **midazolam** > diazepam

| Drug | Potency^A | Onset/ Peak Effect^B | Duration^B |
|-------------|---------------------------------|---|-----------------------------|
| Diazepam | - | Onset: 3-10 min. Peak: 30 min. | 1 - 8 hours |
| Midazolam | 3-4 times as potent as diazepam | Onset: 1-5 min. Peak: 5-10 min. | 0.5 - 2 hours |
| Lorazepam | 5 times as potent as diazepam | Onset: 3-7 min. Peak: 10-20 min. | 6 - 8 hours |

^A 10mg diazepam = 2-3 mg midazolam = 2mg lorazepam

^B IV Administration

Drug Interactions and Precautions With Benzodiazepines:

- Additive therapeutic (sedation) and adverse (respiratory depression) effects can occur when benzodiazepines are administered with opioids or other CNS depressants. Avoid the concomitant use of other CNS depressants when possible; if used in combination, **reduce the dose of the benzodiazepine**.
- Additive therapeutic (sedation) and adverse (respiratory depression) effects can occur when benzodiazepines are administered with the long-acting CNS depressant diphenhydramine (Benadryl). **Avoid the concomitant use of diphenhydramine when possible; if used in combination, reduce the dose of both the benzodiazepine and the diphenhydramine**.
- The danger of apnea from midazolam is greatest in elderly, debilitated patients, patients with chronic disease states or patients with decreased pulmonary reserve. **Titrate midazolam in smaller dosage increments, make sure the rate of injection is slow (> 2 minutes) and wait an appropriate amount of time (at least 3 minutes) before administering additional doses**.
- Benzodiazepines can cause fetal harm, specifically congenital malformations. **Benzodiazepines are contraindicated during pregnancy**.

- Lorazepam and diazepam can also cause venous irritation and thrombophlebitis. Lorazepam must be diluted with an equal volume of diluent such as sterile water, 5% dextrose in water or sodium chloride for IV push administration.
- Prolonged sedation with benzodiazepines can occur with clozapine, cimetidine, ciprofloxacin, saquinavir, retonavir, diltiazem, erythromycin, ketoconazole, itraconazole, high-dose fluconazole, voriconazole and phenytoin.
- Reduced effects of benzodiazepines may occur with rifampin and St. John's Wort.

Special Considerations For Elderly Patients:

- There can be a clinically apparent age-related increase in potency, **time to onset of full therapeutic effect** and duration of action of benzodiazepines in elderly patients. **Reduce the dose; increase the interval between doses.**

Administering a Combination of an Opioid and a Benzodiazepine

- Slow titration of drugs to the desired effect is key to minimizing complications.
 - Rapid IV administration can be associated with hypotension or respiratory depression.
 - As a reminder, anxiolysis, amnesia, elevation of the pain threshold, mood alteration, stable vital signs and enhanced patient cooperation **are** desired end points of sedation/analgesia.
 - However, oversedation, disorientation, the inability of the patient to cooperate, obtunded protective reflexes and labile vital signs **are not** the end points of sedation/analgesia.
- Benzodiazepines, particularly midazolam, produce dose-dependent decreases in ventilation and tidal volume.
- Opioids also produce a dose-dependent depression of ventilation by a direct depression of brainstem function. Opioids depress the ventilatory response to carbon dioxide. Clinically, depression of ventilation produced by an opioid manifests as a reduced frequency of breathing (which can be to the point of apnea) that is not completely compensated for by an increase in tidal volume.
- **Overall, when combining an opioid and a benzodiazepine, the decrease in respiratory rate that the opioid produces coupled with the decrease in tidal volume that the benzodiazepine produces will increase the risk of respiratory depression in a multiplicative fashion.**
 - Reduce the initial dose of both agents by 25-30%.
 - Since the opioid poses a much greater risk of respiratory depression than the benzodiazepine, administer it first then slowly titrate the benzodiazepine dose.
 - If the initial combination produces excessive sedation, when subsequent doses are required, consider giving the opioid first followed by a further reduced dose of benzodiazepine only if necessary.

Rescue Drugs: Naloxone and Flumazenil

NALOXONE

(Narcan®)

Mechanism of Action:

- Naloxone is an opioid antagonist. It competes with the opioid agonist (e.g. morphine, hydromorphone, fentanyl, meperidine, sufentanil) at the receptor, thereby prohibiting the opioid from exerting an effect.
- Naloxone reverses the pharmacological effects of opioids including sedation, analgesia and respiratory depression.

Adverse Effects:

- Precipitation of **withdrawal syndrome** in patients who are opioid dependent
- "Overshoot" phenomena resulting in:
 1. nausea and vomiting (related to the speed of injection and total dose)
 2. **clinically significant** reversal of analgesia
 3. stimulation of the sympathetic nervous system: (increased BP and HR)
 - ventricular irritability
 - arrhythmias
 - pulmonary edema
 - cardiac arrest

Special Considerations:

- **Naloxone does not shorten the duration of action of narcotics.** The plasma concentration of the opioid at the time the effect of naloxone has terminated determines the level of residual sedation or respiratory depression.
- Reversal of respiratory depression from opioids by naloxone will most likely be accompanied by reversal of analgesia.
- Larger doses of opioids with longer durations of action (e.g. morphine and methadone) necessitate a longer monitoring period after the administration of naloxone.

Elimination Half-life of Opioids

| Drug | Half-life |
|---------------|----------------------|
| Morphine | 1.5-4.5 hours |
| Hydromorphone | 1-3 hours |
| Meperidine | 3-4 hours |
| Fentanyl | 1.5-6 hours |
| Sufentanil | 2-3 hours |
| Naloxone | 30-80 minutes |

- **Any patient that receives naloxone following sedation/analgesia shall have a recovery-monitoring period for a minimum of 2 hours.**

Choosing the Appropriate dose:

- There are many factors that affect the individual's response to naloxone including:
 - the agent being reversed
 - the dose of narcotic administered
 - whether the patient is opioid tolerant
- In selecting the dose, the clinician has to balance the risk of inadequate response against adverse reactions. Naloxone should be titrated to effect.
- Prepare dilute naloxone so that it is immediately available during the procedure. Dilute 1 mL of 0.4mg/mL solution with 9 mL of saline for a final concentration of 40 mcg per mL.
- To reverse excessive sedation and/or respiratory depression if the patient is breathing spontaneously, administer 1 mcg per kg, while providing ventilatory assistance and supplemental oxygen. If the patient is apneic, start with 2 mcg per kg.

FLUMAZENIL

(Romazicon®)

Mechanism of Action:

- Flumazenil is a benzodiazepine antagonist. It competes with the agonist (e.g. midazolam, diazepam, lorazepam) at the receptor, thereby prohibiting the benzodiazepine from exerting an effect.
- Flumazenil reverses the pharmacological effects of benzodiazepines, including sedation, respiratory depression, and cardiovascular depression.

Adverse Effects:

- Nausea, tremors, headache, increased sweating, blurred vision, emotional lability, and anxiety (minimized by administering flumazenil in incremental doses and titrating to desired level of sedation)
- Seizures, primarily in patients that:
 - have been taking chronic benzodiazepines
 - have been taking benzodiazepines for epilepsy
 - had a combined overdose of tricyclic antidepressants and a benzodiazepine
 - have an underlying seizure disorder

Contraindications:

- Patients who are receiving benzodiazepines for control of potentially life-threatening conditions and patients who are showing signs of serious tricyclic antidepressant overdose should not receive flumazenil.

Choosing the dose of Flumazenil to minimize adverse effects:

- Flumazenil has an onset of action of 1-3 minutes and a peak effect at 6-10 minutes.
- Titrate dose carefully starting with the smallest recommended dose (0.2 mg) over 15 seconds. Repeat every 2-3 minutes to a maximum of 1 mg.
- If resedation occurs, repeat as above.
- **Flumazenil does not shorten the duration of action of benzodiazepines.** The level of residual sedation is dependent upon the plasma concentration of the benzodiazepine at the time the effect of flumazenil has terminated.
- Larger doses of benzodiazepines that have a longer duration of action (e.g. diazepam and lorazepam) necessitate a longer monitoring period after the administration of flumazenil; repeat doses of flumazenil may be necessary.

Elimination Half-life of Benzodiazepines

| Drug | Half-life |
|-------------|------------------|
| Diazepam | 20 – 80 hours |
| Midazolam | 1.8 – 6.4 hours |
| Lorazepam | 10 – 20 hours |
| Flumazenil | 40 – 80 minutes |

- **Any patient that receives flumazenil following sedation/analgesia shall have a recovery monitoring period for a minimum of 2 hours.**

MEDICATIONS FOR DEEP SEDATION

PROPOFOL (Diprivan®)

Mechanism of Action:

- Propofol is a hypnotic. Its mechanism is not known but may involve GABA receptors, α_2 adrenoreceptors and the N-methyl-D-aspartate subtype of glutamate receptors.
- Propofol has antiemetic effects and produces a sense of well being.
- Propofol has **no analgesic** activity

Adverse Effects:

- Pain at injection site
- Dose-related hypotension, bradycardia
- Apnea
- Anaphylaxis

Contraindications/Precautions:

- Different formulations of propofol have components that can cause allergic reactions. All products contain soybean oil and egg lecithin and some generic products contain sodium metabisulfite.
- Use with extreme caution in patients with cardiac compromise or hypovolemia.

Drug Interactions:

- Propofol potentiates the CNS depression, respiratory depression, and hypotensive effects of barbiturates, benzodiazepines (e.g. Versed®), opioids, phenothiazines, tricyclic antidepressants (e.g. Elavil®)

Special Considerations:

- Use lower initial dose and slower maintenance rate of administration in elderly, debilitated, or ASA III/IV patients
- Follow pediatric dosing recommendations for all pediatric patients

ETOMIDATE (Amidate®)

Mechanism of Action:

- Etomidate is a hypnotic agent. The mechanism of action is similar to propofol in that it is not well defined but seems to involve GABA receptors.
- Etomidate does not have antiemetic properties and does not produce euphoria.
- Etomidate has no analgesic activity.
- Cardiovascular status is relatively **well** maintained while on etomidate.

Adverse Effects:

- Pain at injection site.
- Myoclonus may occur in up to 33% of patients.
- Transient skeletal movements or uncontrolled eye movements may occur in some patients.
- Inhibition of steroid synthesis, which may occur following a single dose.

Contraindications/precautions:

- Use with caution if administering repeated doses in patients with increased intracranial pressure

Special Considerations:

- Use lower initial dose and slower maintenance rate of administration in elderly, debilitated or ASA III/IV patients
- Follow pediatric dosing recommendations for pediatric patients.

METHOHEXITALI (Brevitol®)

Barbiturates have a narrow therapeutic index and may cause apnea at sedative doses. In general, other sedatives are preferred for procedural sedation.

Mechanism of Action:

- Methohexital is a hypnotic barbiturate.
- It affects GABA_A receptors, inhibiting excitatory neurotransmitters and enhancing inhibitory neurotransmitters.
- Methohexital has **no analgesic** activity.

Adverse Effects:

- Pain and rarely necrosis at injection site.
- Dose-related hypotension
- Dose-related apnea
- Anaphylaxis

Contraindications/Precautions:

- Use caution in patients with cardiac compromise or hypovolemia.
- **Porphyria**
- Hepatic dysfunction

Drug Interactions:

- Methohexital potentiates the CNS depression, respiratory depression and hypotensive effects of other barbiturates, benzodiazepines (e.g. Versed), opioids, phenothiazines (e.g. Prochlorperazine), tricyclic antidepressants (e.g. Elavil).

Special Considerations:

- Use **lower** initial dose and slower maintenance rate of administration in elderly, debilitated, or ASA III/IV patients.
- Follow pediatric dosing recommendations for pediatric patients.

KETAMINE (Ketalar®)

Mechanism of Action:

- An agonist at CNS muscarinic acetylcholine-receptors and opiate-receptors that suppresses the pathways involved in pain perception
- Produces dissociative anesthesia, but profound analgesia and near normal pharyngeal-laryngeal reflexes

Adverse Effects:

NOTE: Frequent adverse effects limit the usefulness of ketamine in adults:

- Hypertension, tachycardia, increased cardiac output
- Respiratory depression especially with high dose or too rapid rate of administration
- Vivid dreams, visual hallucinations
- Tremors
- Rash
- Emergence reactions
- Hyperreactive pharyngeal reflexes and excessive salivation (especially in children)
-

Contraindications:

- Contraindicated in patients with high blood pressure
- Contraindicated in patients for whom a significant rise in blood pressure may prove hazardous (e.g. myocardial infarction, or stroke)
- Contraindicated in patients with elevated intracranial pressure
-

Drug Interactions:

- Barbiturates, narcotics, and hydroxyzine prolong recovery time
- NOTE: DO NOT USE KETAMINE in patients with chronic alcoholism or in acutely alcohol-intoxicated patients as these patients may become violent
-

Special Considerations:

- Ketamine has no special precautions for pediatric patients (use weight appropriate dose).
- Reduce the dose for elderly patients

Vasoactive Medications

EPHEDRINE

Use in Procedural Sedation:

- Ephedrine is an alpha-beta adrenergic agent that increases both blood pressure and heart rate. It is useful during procedural sedation to maintain blood pressure. The duration of effect after IV administration is approximately 15 minutes.
- In a patient receiving a beta blocker the alpha effects of ephedrine predominate.
- Administer 5-10 mg IV every 15 minutes as needed for hypotension. The maximum dose in 24 hours is 150 mg; some sources use a maximum per procedure of 50 mg.
- Treat the underlying cause of the hypotension.

PHENYLEPHRINE (Neo-Synephrine)

Use During Procedural Sedation:

- Phenylophrine has direct alpha adrenergic agent activity. Therefore, it is most useful in a patient that is hypotensive and tachycardic (as opposed to hypotensive and bradycardic). It may cause reflex bradycardia.
- To administer phenylephrine, dilute 10 mg in 100 mL to produce a solution with a concentration of 100 mcg/mL. Administer 50 to 100 mcg every 15 minutes as needed, while treating the causes of the hypotension. The duration of effect after IV administration is approximately 15 minutes.

ATROPINE

Use During Procedural Sedation:

- Atropine is an anti-muscarinic anti-cholinergic agent that increases heart rate.
- Administer 0.4-1 mg every 5 minutes, not to exceed a total of 3 mg or 0.04 mg/kg.
- Titrate to effect
- Adverse effects include confusion, hyperthermia and supraventricular tachycardias, all of which are direct extensions of its pharmacologic effect

GLYCOPYRROLATE

Use During Procedural Sedation:

- Glycopyrrolate is an anti-muscarinic anti-cholinergic agent that increases heart rate to a lesser degree than does atropine. Therefore, it may be preferable for patients with coronary artery disease.
- It is slower in onset than atropine
- The dose is 0.2 mg IV, every 2-5 minutes as needed
- Adverse effects include direct extensions of its anticholinergic activity

Documentation requirements post procedure

- You must complete a procedure note, which includes the patient's tolerance of the procedure and relevant information about any problems and interventions during sedation, such as unintended deep sedation or unconsciousness, use of reversal agents, oxygen desaturation, cardiorespiratory decompensation.
- Although post-procedure monitoring is generally provided by the nursing staff, the physician must be sure that the patient will remain under continuous monitoring until the vital signs, oxygen saturation, and level of consciousness are stable compared to pre-sedation baseline state.
- In order to be discharged, the ambulatory patient must be able to maintain a patent airway independently, manage oral secretions or demonstrate the ability to swallow, demonstrate an active gag reflex if appropriate, and have the ability to move and ambulate safely or consistent with pre-procedure status.
- Any patient who received naloxone or flumazenil following sedation/analgesia should be monitored for at least two hours.

REMEMBER: The half-life of the antagonist is shorter than that of the agonist.

- If the patient is an outpatient, the patient will be sent home with Post Sedation Instructions, which include activity restrictions for up to 24 hours.

Patients must have adult supervision for 24 hours.

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