- Dexmedetomidine is the first selective a2-adrenoreceptor agonist approved for short-term (less than 24 hours) infusion as a sedative for patients receiving mechanical ventilation.
- Dosage reduction is recommended with hepatic but not renal impairment.
- Hypotension or bradycardia appears to be most frequent in patients with cardiac conduction defects or hypovolemia. Some patients cannot tolerate the 1 µg/kg loading infusion of dexmedetomidine; for these patients, therapy may be initiated with a maintenance infusion (0.2 to 0.7 µg/kg/hour) that can be titrated to desired effects.
- This drug exerts sedative effects via postsynaptic activation of a2-adrenoreceptors in the CNS and analgesic action by inhibiting norepinephrine release presynaptically. In addition, it inhibits sympathetic activity, thereby decreasing blood pressure and heart rate. Dexmedetomidine is eight times more potent than its relative, clonidine, at stimulating a2-adrenoreceptors.
- Dexmedetomidine offers several advantages as a sedative in the ICU. (i) It does not cause significant respiratory depression (ii) It has a rapid distribution phase (6 minutes) and an elimination half-life of 2 hours. These pharmacokinetic properties permit easy dose titration in response to fluctuating sedative needs. (iii) Another advantage is the low level of sedation that can be achieved with dexmedetomidine. Patients appear comfortably sedated while undisturbed but can easily be awakened. (iv) Dexmedetomidine has also been used successfully to ameliorate the hyperadrenergic state of drug withdrawal caused by alcohol, illicit drugs, or long-term sedative-analgesic use in the ICU.
- Because dexmedetomidine is approved for use only for 24 hours, further pharmacokinetic, pharmacodynamic, and clinical research is necessary before it can be recommended for long-term use in ICU patients.

- Of the sedative medications discussed in this chapter, BZDs and opioids are most likely to be involved in toxic ingestions, either accidental or intended. Patients with overdoses from either medication class can present with stupor or coma with hypotension (usually mild and responsive to fluid boluses) and hypotonia. Pupil size may be helpful: pupils are pinpoint in opiate ingestion, mid-size in BZD toxicity. Toxicity is usually short-lived and completely reversible unless complications such as anoxic encephalopathy or aspiration pneumonia occur.

- Naloxone can be given as both a diagnostic and therapeutic medication; lack of improvement in level of consciousness or respiratory depression after administration of 10 mg of naloxone (starting with 0.4 mg and giving subsequent doses of 2 mg every few minutes) makes opiate toxicity an unlikely cause of the patient’s symptoms. If a response is observed, then practitioners should be prepared to administer repeated naloxone boluses every 30 to 60 minutes or to start a continuous infusion at 0.4 to 0.8 mg/hour.
- Occasionally, a patient with opiate overdose develops pulmonary edema requiring mechanical ventilation, but the edema usually resolves within a few days without specific treatment.
- Flumazenil is a specific antidote for BZD toxicity. A patient’s symptoms should improve within a minute after a bolus administration of 0.2 mg and subsequent 0.3-mg doses every 30 seconds.
- Administration of flumazenil to patients receiving chronic BZD therapy may precipitate an unpleasant acute withdrawal syndrome and, theoretically, increase the risk of seizure. However, no seizures were observed after flumazenil treatment in 110 patients with suspected BZD overdose, including many patients with polydrug ingestions (e.g., cotreatment with tricyclic antidepressants).

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### Drugs for Overdose

<table>
<thead>
<tr>
<th>Drug</th>
<th>Estimated Sedative Dose</th>
<th>Intravenous Dose</th>
<th>Halflife (h)</th>
<th>Elimination Glucuronidation (%)</th>
<th>Active Metabolites</th>
<th>Special Considerations</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzodiazepines</td>
<td>5-6 mg</td>
<td>0.5-5 mg/kg</td>
<td>2-5</td>
<td>Yes</td>
<td>0.030-0.1 mg/kg</td>
<td>Histamine release can cause hypotension and cardiovascular instability</td>
<td></td>
</tr>
<tr>
<td>Meprobamate</td>
<td>50-150 mg</td>
<td>0.5-5 mg/kg</td>
<td>1-2</td>
<td>None</td>
<td>0.040-0.5 mg/kg</td>
<td>$6</td>
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</tr>
<tr>
<td>Propofol</td>
<td>50-150 mg</td>
<td>0.5-5 mg/kg</td>
<td>1.5</td>
<td>None</td>
<td>0.040-0.5 mg/kg</td>
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<tr>
<td>Dexmedetomidine</td>
<td>0.5-10 µg/kg</td>
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### Indications and Comments

- **Minimize ventilatory dysfunction**: Poor synchrony may lead to hypoxemia and dyspnea and is distressing to caregivers. Ventilator adjustment may improve synchrony without medications.
- **Reduce dyspnea associated with severe acute respiratory failure**: Reducing minute ventilation to avoid ventilator-induced lung injury can cause severe dyspnea. Tachypneas with short expiratory times can lead to increased auto-PEEP and hypoxia.
- **Increase tolerance of intubation**: A tracheal cuffed tracheal tube can cause pain, gagging, and reflex brong. Local anesthesia can reduce the need for sedatives and analgesics.20
- **Reduce anxiety**: Acute stress theory probably leading to disability or death may produce unwanted psychological distress.
- **Reduce recall of ICU symptoms**: Recall of distressing symptoms such as severe dyspnea, terror, Remit, or pain can have long-term psychological consequences.20
- **Reduce stress response and oxygen consumption**: Reducing unneeded motor activity or respiratory effort can decrease total body oxygen consumption by 15%.20
- **Reduce elevated intracranial pressure**: Coughing, straining, or excessive ventilator dysrhythmia can cause dangerous spikes in intracranial pressure.
- **Reduce pain**: Surgical or traumatic wounds, catheter and tube placement, and immobilization usually cause pain.
- **Prevent removal of life support technology**: Removal of all mechanical tubes in tracheal catheter can cause death within minutes.
- **Induce sleep**: ICU patients often have abnormal chronology cycles associated with delirium and impaired immune function.
- **Increase efficiency of patient care delivery**: Constant visual observation and relief of patient discomfort may be impossible in understaffed units.
- **Protect caregivers from violent behaviors**: Confused patients can violently assault caregivers.
- **Adjust during pharmacologic paralysis**: Awareness during pharmacologic paralysis is unacceptable and can have long-term psychological consequences.
- **Shorten duration of delirium**: Antipsychotics may reduce delirium without affecting consciousness or behavior.
- **Family considerations**: Repeatedly observing the distress of a loved one can cause anguish in family members, who may seek additional sedatives be given to the patient.20

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### therapy for overdose

- Benzodiazepines
- Opioids
- Other agents

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### presentation in overdose

- Sedative hypnotics
- opiates
- benzos