Sedative-Hypnotics
No “best” sedative agent

Any agent given in sufficient dosage can produce any level of sedation

Intravenous dosing is more predictable than intramuscular or oral dosing
Avoiding adverse reactions:

- Establish a desired endpoint for your titration – what are you trying to achieve? For example, sleepy but responsive to a command to open the eyes.
- Wait until full effect is evident (i.e. slowly titrate to effect) before administration/redosing of additional medications.
- As an example, for midazolam, titrating to an endpoint of slurred speech reliably yields amnesia.
Sedative Agents (General Considerations)

Adverse reactions are more common with:

- Hepatic or renal insufficiency
- Decreased cardiac or respiratory function
- Obesity
- Sleep Apnea
- Concurrent use of other sedating agents (e.g. anticonvulsants or antihistamines)
Benzodiazepine Effects

- Anxiolysis/Sedation/Hypnosis
- Produce anterograde amnesia
- Minimal respiratory depression if given alone at normal sedative ranges
- Anti-convulsant
- Anti-spasmodic
Diazepam

- Painful IV injection
- Relatively fast onset
- Increased response to a given dose or prolonged duration of action occur with
  - Liver disease
  - Renal failure
  - Hypoalbuminemia
  - Patients taking cimetidine
  - Elderly patients
- Very long elimination half life and active metabolites

- **Effects**
  - Airway compromise at >0.3 mg/kg
  - Cardiovascular depression at >0.5 mg/kg
  - Somnolence within 0.5 - 1 hr and up to 6-8 hrs after PO dose
Midazolam

• Water soluble – does not burn on injection
• Very fast onset
• Increased response to a given dose or prolonged duration of action occur with:
  • Liver disease
  • Renal failure
  • Hypoalbuminemia
  • Patients taking ketoconazole, erythromycin, diltiazem, verapamil, and cimetidine
  • Elderly patients

➢ Short acting: normal mentation after 4 hrs.
➢ AGENT OF CHOICE FOR PROCEDURAL/TEST SEDATION
➢ Effects:
  • 2-3 times more potent than diazepam
  • More potent amnestic agent than diazepam
  • Airway compromise (often mimics respiratory depression) at >0.15 mg/kg
  • Cardiovascular depression at >0.2 mg/kg
Lorazepam (Ativan)

- Slow onset (10 minutes)
- Increased response to a given dose or prolonged duration of action occur with:
  - Liver disease
  - Renal failure
  - Hypoalbuminemia
  - Patients taking clozapine and haloperidol
  - Elderly patients
- Long acting
- FDA says to avoid in outpatient endoscopic procedures

OUR SUGGESTION IS NOT TO USE THIS DRUG FOR PROCEDURAL OR TEST SEDATION
# Sedative Dosing

<table>
<thead>
<tr>
<th>Sedative-Hypnotics</th>
<th>Dose</th>
<th>Times</th>
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</thead>
<tbody>
<tr>
<td><strong>Diazepam</strong></td>
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<tr>
<td>IV: 1-5 mg titrate</td>
<td></td>
<td>IV Onset: 3-5 min</td>
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<tr>
<td>PO: 1-5 mg titrate</td>
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<td>Duration: 2-8 hr</td>
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<tr>
<td>IM: 1-5 mg titrate</td>
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<td></td>
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<tr>
<td>Max 5 mg for elderly and debilitated</td>
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<tr>
<td><strong>Midazolam</strong></td>
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<tr>
<td>IV: 0.5-1 mg until desired effect is achieved.</td>
<td>IV Onset: 1-2 min</td>
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<tr>
<td>PO: 0.5-0.8 mg/kg</td>
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<td>Duration:</td>
</tr>
<tr>
<td>IM: 0.02-0.1 mg/kg</td>
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<td>IV PEAK EFFECT 5 min</td>
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<tr>
<td>Max 50 mg</td>
<td></td>
<td>IV Recovery 30-40 min</td>
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<td>IV Total recovery 6 hr</td>
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</tbody>
</table>
Flumazenil

- Specific benzodiazepine competitive antagonist
- Should NOT be used to routinely reverse sedation
- May precipitate withdrawal syndrome if used in patients taking chronic benzodiazepines
- IV 8-15 mcg/kg onset 1-2 minutes, reverses CNS effects in 6-8 minutes
- Action is shorter than benzodiazepine effects. Therefore all patients who receive reversal agents must be monitored at least 2 hours after the last dose of flumazenil
- May cause:
  - seizures, cardiac arrhythmias and death
  - anxiety, dizziness, sweating and emotional liability
<table>
<thead>
<tr>
<th>Flumazenil</th>
<th>Dose</th>
<th>Times</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>IV:</strong> 0.2 mg, may repeat up to 4 times q60 sec</td>
<td><strong>Onset:</strong> 1-2 min Peak in 6-8 min</td>
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<td></td>
<td><strong>Max:</strong> 1 mg</td>
<td><strong>Duration:</strong> 30-60 min</td>
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<td>May repeat treatment regimens at 20 minute intervals</td>
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<td></td>
<td><strong>IM/SC:</strong> 0.1-0.2 mg, Max 1 mg</td>
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