Analgesics
Opioid Definition

- All drugs, natural or synthetic, that bind to opiate receptors
  - Agonists: morphine, fentanyl
  - Agonists-Antagonists: nalbuphine
  - Antagonists: naloxone

- Opioid agonists increase pain threshold by altering the perception of noxious stimuli

- Opioids are more effective if given before the stimulus occurs
Opioid CNS Effects

- Analgesia
- Sedation
- Euphoria, occasionally dysphoria
- Miosis (small pupils)
- Nausea and vomiting
- Depressed cough
Opioid Cardiovascular Effects

- Bradycardia
- Hypotension
- Histamine release (morphine)
Opioid Respiratory Effects

- Dose dependent respiratory depression: decreased respiratory rate
- Increased CO$_2$ retention
- Decreased cough reflex
- Bronchospasm due to histamine release (morphine)
Other Opioid Effects

- Urinary retention
- Chest wall rigidity (may make ventilation difficult)
- Miosis
- Biliary tract spasm
- Pruritus
- Decreased GI motility (delayed gastric emptying, ileus and constipation)
Opioid Overdose

- **Signs and symptoms**
  - Respiratory depression
  - Hypotension
  - Loss of consciousness

- **Treatment**
  - Ventilatory support
  - Intravascular volume
  - Naloxone titration
Morphine

- Naturally occurring opioid
- Lipid insoluble: slow onset
- Hepatic metabolism
- 15% excreted unchanged by kidney
- Causes histamine release: bronchospasm and hypotension
Morphine

- Decreased metabolism in liver failure
- Decreased excretion of morphine and its active metabolites in renal failure (increased effects and present up to 7 days)
- Larger effect in the elderly for a given dose
Meperidine (Demerol)

- 1/10 potency of morphine
- 90% hepatic metabolism
- Metabolite normeperidine can cause seizures with prolonged (days) use. This risk is increased if there is renal failure

Analgesics
- 75-100 times more potent than morphine
- Highly lipid soluble:
  - Faster analgesic effect
  - Faster onset of respiratory depression
- Short acting
- End of action unrelated to liver or renal function
# Opioid Dosing

<table>
<thead>
<tr>
<th>Drug</th>
<th>Adult Dosing</th>
<th>Onset/Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Morphine sulfate</strong></td>
<td>IV: 1-2 mg increments Max 15-20 mg</td>
<td>Onset: 3-5 min</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Peak: 10-15 min</td>
</tr>
<tr>
<td><strong>Meperidine</strong></td>
<td>IV: 10 mg increments Max 50-150 mg</td>
<td>Onset: 3-5 min</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Peak: 10-15 min</td>
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<tr>
<td><strong>Fentanyl</strong></td>
<td>IV: 0.05 ug/kg increments Max: 2 ug/kg</td>
<td>Onset: 1-3 min</td>
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<tr>
<td></td>
<td></td>
<td>Peak: 3-5 min</td>
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</tbody>
</table>

- Titrate to Effect
- Decrease Doses 25% with Benzodiazepines
Opioid Dosing Caveats

- Maximum doses are for those not on chronic opioids
- Titrate to effect at all times
  - Wakefulness
  - Respiratory rate
  - Level of Analgesia
- Must make sure that treating “pain” is not treating hypoxemia induced combativeness

THIS IS A COMMON CAUSE OF DEATH IN SEDATION ANALGESIA
Opioid Drug Interactions

- Additive CNS depression when combined with other CNS active agents
- Vagolytic drugs counteract bradycardia
- MAO inhibitors and tricyclic antidepressants increase duration of action, respiratory depression and incidence of seizures
- Meperidine should not be given concomitantly MAOIs
Opioid Antagonists: Naloxone

- Competitive antagonist at mu, kappa and sigma receptors, reversing all effects
- Titrate to effect
- Acts within 1-2 mins for 1 hr only
- May cause large sympathetic discharge
  - Severe hypertension and tachycardia
  - Pulmonary edema
  - Cardiac arrest
Opioid Reversal Agents

- Use with extreme caution in patients on chronic opioid therapy as may cause severe physical withdrawal syndrome.
- Opioid effects may outlast reversal effects: the action of naloxone lasts 30-45 mins.
- Patients receiving reversal should be monitored at least 3 hrs. after last dose.
Opioid Reversal Agents

Reversal agents: monitor patients at least 4 hs after administration

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<tr>
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<th>Onset/Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Naloxone</td>
<td>IV: 0.1 to 0.2 mg slow and titrate to response</td>
<td>Onset: 1-2 min</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Duration: 30 min when given IV</td>
</tr>
</tbody>
</table>
| Nalmefene (Revex) | IV: 0.25 ug/kg  
May repeat at 2 and 5 mn  
Max: 1 ug/kg | Duration: half life is 9 times longer than Narcan    |

Analgesics