Intravenous Nonopioid Anesthetics
Agents

"The broad class of intravenous anesthetics can be broken down into opioids (also known as narcotics), non-opioids and muscle relaxants. While there are many drugs that can be used intravenously to produce anesthesia or sedation, the most common IV non-opioid anesthetics are:

1) Barbiturates
   • Amobarbital (trade name: Amytal)
   • Methohexital (trade name: Brevital)
   • Thiamylal (trade name: Surital)
   • Thiopental (trade name: Pentothal, referred to as thiopentone in the UK)

2) Benzodiazepines
   • Diazepam (Valium)
   • Lorazepam (Ativan)
   • Midazolam (Versed)

3) Etomidate (Amidate)

4) Ketamine

5) Propofol

The two barbiturates mentioned above, thiopental and methohexital, are ultra-short-acting, and are used to induce and maintain anesthesia. However, though they produce unconsciousness, they provide no analgesia (pain relief) and must be used with other agents. Until recently, the most commonly used intravenous induction agents were the barbiturates. Thiopental provides rapid onset and offset when used as a single dose, but it accumulates rapidly with prolonged administration and leads to slow recovery. Methohexital has a rapid onset and offset similar to propofol for procedures lasting under 2 hours. The barbiturates are administered as sodium salts diluted in a water base at an alkaline pH. Like propofol, the barbiturates are thought to provide their hypnotic effects largely through action on the GABA receptor. Barbiturates provide cerebral protection and are generally used primarily for this purpose. They cause a moderate dose-dependent
decrease in blood pressure (primarily as a result of peripheral vasodilation) and respiratory drive. The barbiturates are contraindicated in patients with porphyria. The induction dose of thiopental is 4 mg/kg, and that for methohexital is 2 mg/kg. Methohexital can be used for maintenance of anesthesia at 100 to 200 µg/kg/min or for conscious sedation at 25 to 75 µg/kg/min. The introduction of thiopental into clinical practice in 1934 marked the advent of modern intravenous anesthesia. Today, intravenous anesthetics are used for induction of anesthesia, maintenance of anesthesia, and provision of conscious sedation.

**Benzodiazepines** can be used for sedation before or after surgery and can be used to induce and maintain general anesthesia. When benzodiazepines are used to induce general anesthesia, midazolam is preferred. Benzodiazepines are also used for sedation during procedures that do not require general anesthesia. Like barbiturates, benzodiazepines have no pain-relieving properties. The benzodiazepines are used primarily as premedicants for anxiolysis and amnesia or for conscious sedation. The water-soluble benzodiazepine midazolam is the most frequently used intravenously because of its relatively rapid onset and offset and lack of active metabolites when compared with other benzodiazepines (e.g., diazepam). The onset of midazolam is slower than that of both propofol and barbiturates, and its offset, especially when used at higher doses or in a prolonged infusion, is considerably longer than that of propofol or methohexital. The benzodiazepines act through the GABA receptor. Flumazenil is a specific benzodiazepine antagonist. It can be used to reverse the effects of benzodiazepines. In general, the benzodiazepines produce only a mild decrease in blood pressure and mild to moderate respiratory depression. The dose of midazolam for anxiolysis and mild sedation is 0.015 to 0.03 mg/kg intravenously and is generally repeated in 30 to 60 minutes as needed.

**Propofol** is one of the most commonly used intravenous drugs employed to induce and maintain general anesthesia. It can also be used for sedation during procedures or in the ICU. Like the other agents mentioned above, it renders patients unconscious without producing pain relief. Propofol is an alkylphenol presently formulated in a lipid emulsion. Propofol provides rapid onset and offset with context-sensitive decrement times of approximately 10 minutes when infused for less than 3 hours and under 40 minutes when infused for up to 8 hours. Its mechanism of action is thought to be potentiation of GABA-induced chloride currents. At therapeutic doses, propofol produces a moderate depressant effect on ventilation. It causes a dose-dependent decrease in blood pressure primarily through a decrease in cardiac output and systemic vascular resistance. A unique action of propofol is its antiemetic effect, which remains present at concentrations below those producing sedation. The induction dose is 1 to 2 mg/kg for loss of consciousness with a maintenance infusion of 100 to 200 µg/kg/min. For conscious sedation, rates of 25 to 75 µg/kg/min are usually adequate.

Because of its favorable physiological effects, "etomidate has been primarily used in sick patients". **Etomidate** is an imidazole derivative used primarily for induction of anesthesia, especially in the elderly and patients who are cardiovascularly compromised. It has a rapid onset of effect and a rapid offset even after a continuous infusion. However,
prolonged infusion results in inhibition of adrenocortical synthesis and potential mortality in ICU patients. The major advantage of etomidate is its minimal effect on the cardiovascular and respiratory systems. It is associated with a high incidence of burning on injection, thrombophlebitis, and postoperative nausea and vomiting, thus limiting its popularity. The induction dose is 0.2 to 0.3 mg/kg.

**Ketamine** is a dissociative anesthetic developed in 1963 to replace PCP and currently used in human anesthesia and veterinary medicine. It is infrequently used in anesthesia because of the unpleasant experiences that sometimes occur on emergence from anesthesia, which include "vivid dreaming, extracorporeal experiences, and illusions." However, like etomidate it is frequently used in emergency settings and with sick patients because it produces fewer adverse physiological effects. Unlike the intravenous anesthetic drugs previously mentioned, ketamine produces profound pain relief, even in doses lower than those that induce general anesthesia. Also unlike the other anesthetic agents in this section, patients who receive ketamine alone appear to be in a cataleptic state, unlike other states of anesthesia that resemble normal sleep. Ketamine-anesthetized patients have profound analgesia but keep their eyes open and maintain many reflexes. Ketamine is a phencyclidine derivative that has been used for both induction and maintenance of anesthesia. Ketamine acts primarily, but not entirely through the NMDA receptor. It provides both a dissociative state of hypnosis and analgesia. Ketamine is associated with significant adverse psychological effects at higher doses, as well as several other side effects. Thus, more recently it is used primarily for its analgesic properties. It has rapid onset and relatively rapid offset, even after an infusion of several hours. It has sympamathomimetic action that preserves cardiac function. Ketamine has minimal effect on respiration and tends to preserve autonomic reflexes. The induction dose is 2 to 4 mg intravenously. An infusion of ketamine will provide analgesia and can be given with propofol in a total intravenous anesthesia technique. A dose of 10 to 20 mg preoperatively has been shown to provide preemptive analgesia.

**Other Intravenous Nonopioid Anesthetics Agents**

1. **Dexmedetomidine (Precedex)** is the most recently released intravenous anesthetic. It is a highly selective α2-adrenergic agonist that produces sedation, hypnosis, and analgesia. Dexmedetomidine is presently approved only for brief (<24 hours) postoperative sedation. Its primary action is on α2-receptors in the locus ceruleus. It has minimal effect on respiration. Dexmedetomidine produces a biphasic effect on blood pressure: at low concentrations mean blood pressure is decreased, and at higher concentrations, blood pressure is increased. Heart rate and cardiac output show a concentration-dependent decrease. Dosing for sedation
is a loading dose of 2.5 to 6.0 µg/kg over a 10-minute period, followed by an infusion of 0.1 to 1 µg/kg/hr.

2. Droperidol, a butyrophenone and major tranquilizer, was initially used to produce a state of neuroleptanesthesia. It is an antidopaminergic drug that is also used as an antiemetic and antipsychotic. Recent concern regarding its effect on prolonging the QT interval has resulted in its withdrawal in several countries and its limitation to the treatment of postoperative nausea and vomiting with a black box warning in the United States regarding the potential for sudden cardiac death at high doses (>25 mg) in psychiatric patients. Prolongation of the QT interval by doses used for postoperative nausea and vomiting (0.625 to 1.25 mg) has been challenged by several editorials, and this effect has not been substantiated by review of the cases reported or any literature. Droperidol at low doses remains one of the most effective antiemetic therapies available”.

Sources combined:
