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Pharmacology II

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Drug Therapy with Local Anesthetics

Local anesthetics, given to produce loss of sensation and motor activity, are injected into localized areas of the body. These agents decrease the permeability of the nerve cell membrane to ions, especially sodium. They stop the nerve from depolarizing, preventing the sodium ions from entering the nerve, which means that the nerve impulses can no longer be initiated or conducted by the anesthetized nerves. Thus, local anesthetics prevent the cells from **responding to pain impulses and sensory stimulation**. This loss of sensation occurs in the following sequence: **temperature**, **touch**, **proprioception**, and **skeletal muscle tone**. These effects diminish as the drug molecules diffuse out of the neurons into the bloodstream. The drugs are then transported to the liver for metabolism to inactive metabolites and eventual excretion in the urine.

Methods of Administration

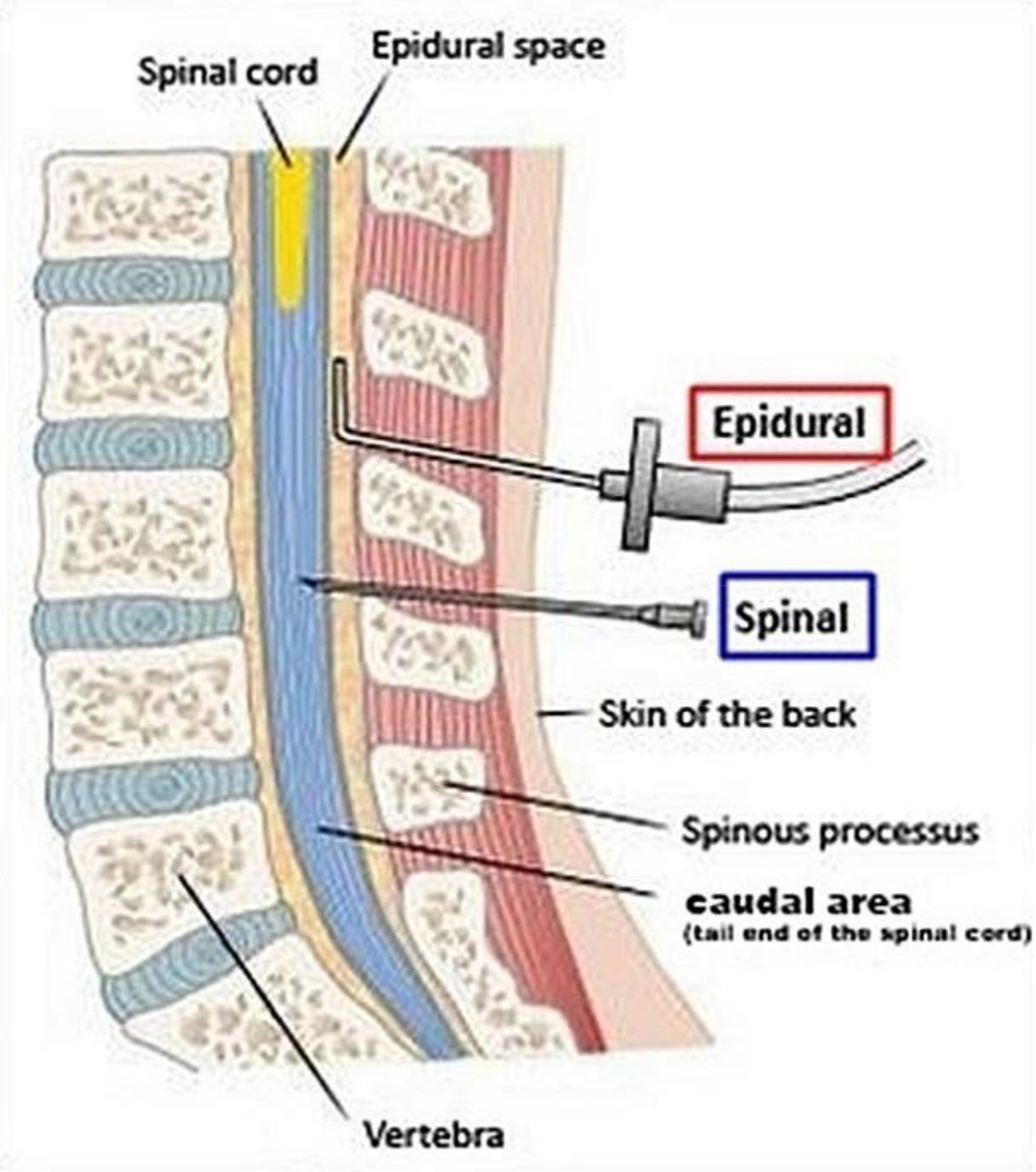
There are several different methods to administer local anesthesia.

Topical anesthesia involves the application of ointment, lotion, cream, or drop of local anesthetic to the skin or mucous membranes in the eyes, nose, throat, mouth, urethra, anus, or rectum. These preparations are used to relieve pain and itching of dermatoses, sunburn, minor skin wounds, hemorrhoids, sore throat, and other conditions.

Field block anesthesia is where nerves are blocked en masse by an anesthetic agent, not individually, to form a barrier proximal to the surgical site. This method is often used for tooth extraction.

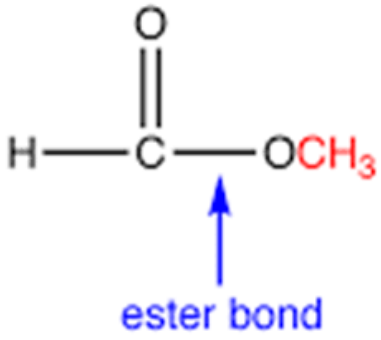
Nerve block anesthesia involves blocking a group of nerves, called a plexus or ganglion, through the injection of an anesthetic into a specific area of the body.

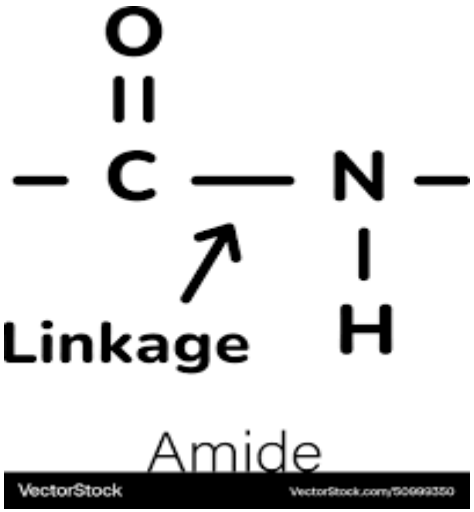
Neuraxial blocks are epidural, spinal, and caudal. Peripheral nerve blocks involve blocking a single nerve or group of nerves such as a plexus or ganglion


Spinal cord
Epidural space
Epidural
Spinal
Skin of the back
Spinous processus
caudal area
(tail end of the spinal cord)
Vertebra

The local anesthetic agents are classified as amides and esters. The molecular structure of the amides possesses an amide linkage, and the esters' structure contains an ester linkage. The amide group is the most commonly used clinically.

Drug Class	Prototype	Other Drugs in the Class
Amides	Lidocaine (ReadySharp Lidocaine, Xylocaine)	Bupivacaine (Exparel, Marcaine, Sensorcaine) Liposomal Bupivacaine (Exparel) Dibucaine (Nupercaine) Mepivacaine (Carbocaine, Polocaine) Ropivacaine (Naropin)
Esters	Chloroprocaine (Clorotekal Nesacaine, Nesacaine-MPF)	Benzocaine (Anacaine, Anbesol, Benz-O-Sthetic, Blistex, Cepacol, Dentapaine, Topex Topical Anesthetic) Tetracaine hydrochloride





Lidocaine (Xylocaine) is the prototype amide local anesthetic agent. The drug has a rapid effect, and when combined with epinephrine, this effect is prolonged.

Topical preparation: used to relieve pain associated with post herpetic neuralgia

Injectable solution: used for infiltration of the skin or subcutaneous administration prior to the insertion of an IV or central venous catheter, spinal, epidural, or a minor emergency procedure such as suturing or aminor surgical procedure.

Drug	Pregnancy Category	Routes and Dosage Ranges	
		Adults	**Children**
Lidocaine (ReadySharp Lidocaine, Xylocaine; Cathejell, Jelido, Lidodan, Xylocaine)	B	Maximum single dose, 300 mg, with epinephrine 500 mg; do not repeat within 2 h Infiltration, 0.5% or 1% Peripheral nerve block, 1% or 2%, 3–40 mL Epidural, 1%, 1.5%, or 2%, 20–30 mL in 3–5 mL increments, allowing time to detect toxic manifestations Saddle block, 1% with dextrose Topical, 2.5%–5% jelly, ointment, cream, solution	Anesthesia, local injectable, 5 mg/kg/dose not to exceed adult maximum dose of 300 mg/dose; do not repeat within 2 h; administer lowest concentrations to allow for larger volumes
Bupivacaine (Exparel, Marcaine, Sensorcaine, Bupivacaine Spinal; Marcaine, Sensorcaine)	C	Maximum single dose, 175 mg, with epinephrine 200 mg Local anesthesia, 0.25% Spinal, 0.75% in 8.25% dextrose, 1–2 mL Epidural, 0.25% or 0.5%, 20–30 mL in 3–5 mL increments, allowing time to detect toxic manifestations Caudal, 0.25% or 0.5%, 15–30 mL Peripheral nerve block, 0.25% or 0.5%, 3–40 mL	≥12 y, same as adults Caudal, 0.25%, 0.5–1.25 mL/kg, not to exceed 2.5 mg/kg
Mepivacaine (Carbocaine, Polocaine, Scandonest Plain; Carbocaine, Polocaine)	C	Maximum single dose, 300 mg, with epinephrine 500 mg Infiltration, 0.5% or 1%, up to 40 mL of 1% solution Therapeutic block pain management, 1–5 mL of 1% solution (max dose 50 mg) Caudal and epidural block, 15–30 mL of 1% solution (max 300 mg) or 10–25 mL solution (max 375 mg) or 10–20 mL of 2% solution (max 400 mg)	Local or regional anesthesia: max single or total dose for one procedure 5–6 mg/kg (to adult max); only concentration <2% should be used in children <3 y or <14 kg
Ropivacaine (Naropin; Naropin)	B	Maximum single dose, 200 mg, with epinephrine 250 mg Infiltration, 0.2% or 0.5% Epidural, 0.5%, 0.75%, or 1%, 15–30 mL Peripheral nerve block, 0.5% or 0.75%, 10–40 mL	Caudal, 0.2%, 0.5–1.25 mL/kg, not to exceed 2 mg/kg Epidural, 0.2%, 0.7 mL/kg (wait 45 min for repeat dosing, reduce dose by 1/3–1/2)

Chloroprocaine hydrochloride serves as the prototype ester local anesthetic. The decreasing use of the esters has significantly decreased the frequency of anaphylaxis with local anesthetics as most allergic reactions are due to para-aminobenzoic acid, the common metabolic product of esters.

Drug	Pregnancy Category	Routes and Dosage Ranges	
		Adults	Children
(P) **Chloroprocaine** (Clorotekal, Nesacaine)	C	Max single dose, 800 mg, with epinephrine 1000 mg Infiltration, 1% or 2% Epidural or caudal, 2% or 3%, 15–25 mL Peripheral nerve block, 1% or 2%, 0.5–10 mL	Max dose (without epinephrine), 11 mg/kg Infiltration, 0.5% or 1% Peripheral nerve block, 1%–1.5%
Benzocaine (Anacaine, Anbesol, Benz-O-Sthetic, Blistex, Cepacol, Dentapaine, Topex Topical Anesthetic)	C	Topical anesthesia, 1–2 drops of 0.5% solution or 1.25–2.5 cm of ointment in the lower conjunctival fornix or 0.5% solution or ointment to the nose or throat; spray 5%, 1 spray up to four times daily	Check product insert for pediatric dosage
Tetracaine (Ametop)	C	Topical anesthesia, 1–2 drops of 0.5% solution or 1/25–2.5 cm of ointment in lower conjunctival fornix or 0.5% solution or ointment to nose or throat Spinal anesthesia, 2.5–15 mg; dosage varies with anesthetic procedure	Check product insert for pediatric dosage

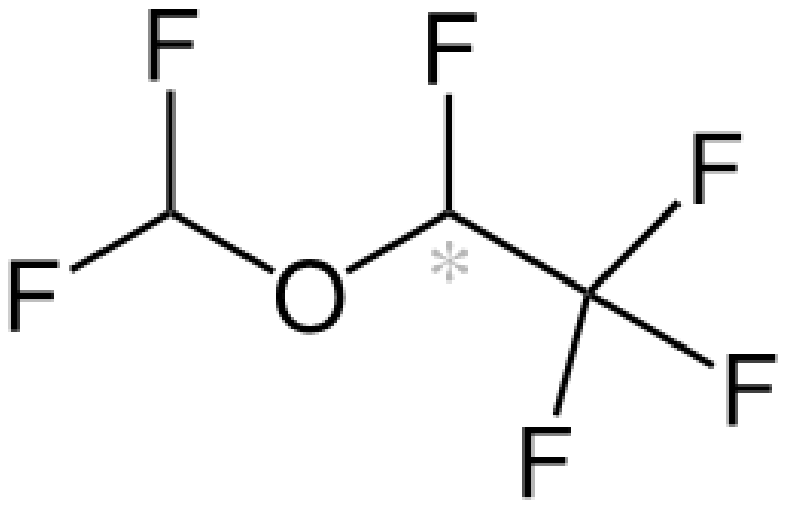
Drug Therapy With General Anesthetics

General anesthesia is defined as a medication-induced reversible unconsciousness with loss of protective reflexes. There is the misconception that **general anesthesia is a deep sleep**. It is much deeper and more like a drug **induced coma**. Arousal, even to painful stimuli, cannot occur. Therefore, it is possible to perform surgery or other unpleasant therapeutic or diagnostic procedures such as endoscopy or interventional radiology that would be unreasonable or impossible to accomplish in a conscious person

❑ Inhalation anesthetics

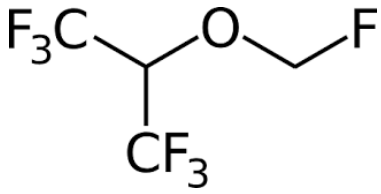
Volatile means having the ability to evaporate readily and release a gas. Today's volatile inhalation anesthetics are **halogenated ethers, which contain fluorine**. They are administered through a face mask, laryngeal mask airway or tracheal tube connected to an anesthetic vaporiser and an anesthetic delivery system. Inhalation anesthetics (**nitrous oxide**, **halothane**, **isoflurane, desflurane, sevoflurane**, most commonly used agents in practice today) are used for induction and maintenance of general anesthesia in the operating room

- **Desflurane** is a completely fluorinated methyl ethyl ether. Patients benefit from **faster recovery** and **return of normal cognition**. However, desflurane is very **pungent**, making mask inhalation induction impractical. Moreover, desflurane produces airway **irritation** and increases the incidence of **coughing**, **breath holding**, or **laryngospasm**. Unlike other inhalation anesthetics, desflurane may cause mild bronchoconstriction.



- **Sevoflurane** is a completely fluorinated methyl isopropyl ether that has about **half** the potency of isoflurane. Its **nonpungent** and results in the **least** amount of airway **irritation**. It provides a pleasant inhalation mask induction in both adults and children without the need of an initial intravenous anesthetic. Furthermore, it produces broncho dilation similar or perhaps greater than isoflurane.
- **Nitrous oxide** the volatile anesthetics , inorganic inhalation agent ,can be used in combination with other anesthetic medications. Also known as **laughing gas**, it is not a volatile agent like isoflurane because it is a gas at room temperature. Unfortunately, the **potency** of nitrous oxide is **low**, and it cannot produce general anesthesia by itself. However, its additive effect will permit a lower concentration or dose of the volatile or intravenous anesthetics.

Nitrous oxide produces amnesia (memory loss), analgesia, and euphoria



❑ Neuromuscular blocking agents

Modern neuromuscular blocking agents, or muscle relaxants, are divided into two classes,

- **nondepolarizing**

Vecuronium, a nondepolarizing aminosteroid compound, is the prototype. There are several nondepolarizing muscle relaxants.

- **depolarizing muscle relaxants**.

Succinylcholine is the only depolarizing agent.

Each agent has unique characteristics and the anesthesia practitioner makes the appropriate choice based on the **health history** of the patient as well as the **length and type of procedure**

Nondepolarizing Neuromuscular Blocking Agents

long-acting (greater than 60 minutes) pancuronium and the intermediate-acting (less than 60 minutes) rocuronium.

Pancuronium is useful when prolonged paralysis is indicated.

Rocuronium has a rapid onset in high doses and is the drug of choice when succinylcholine is contraindicated.

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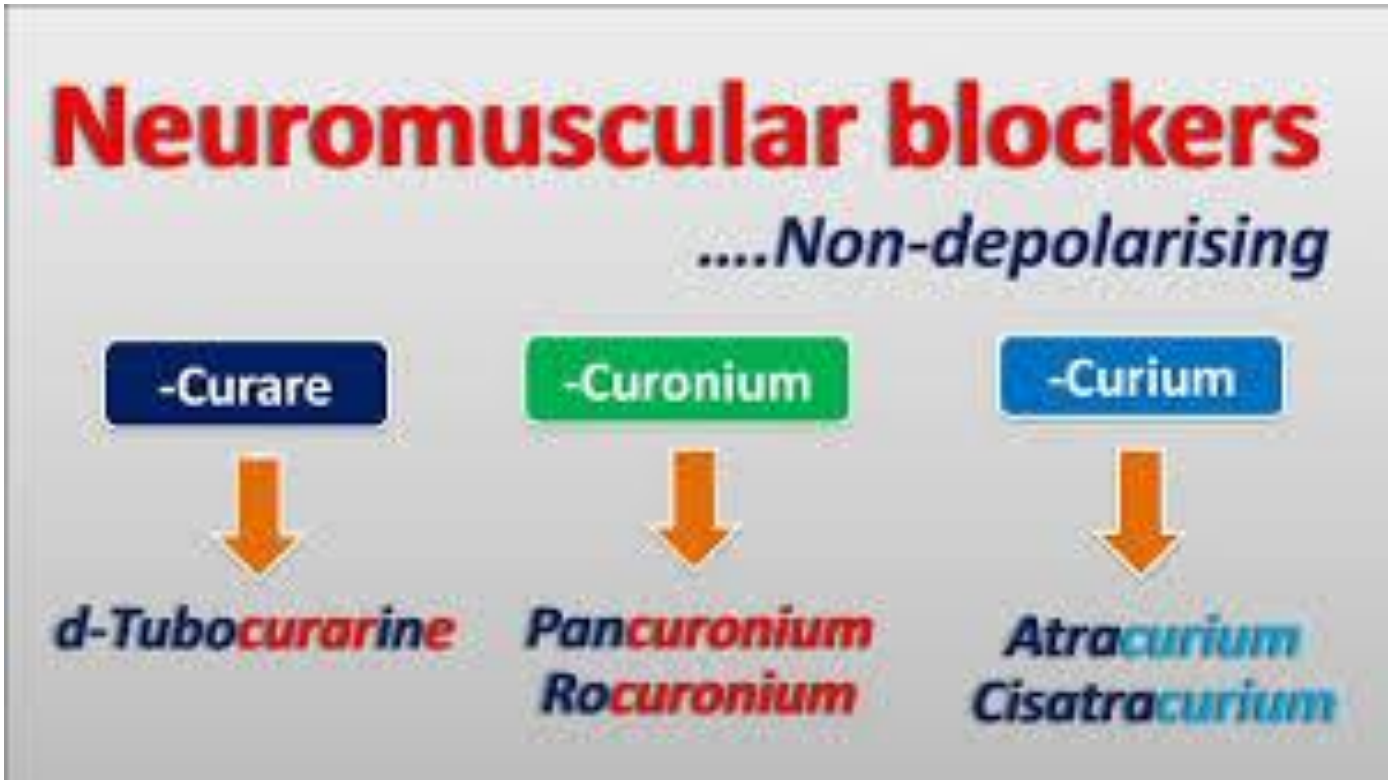
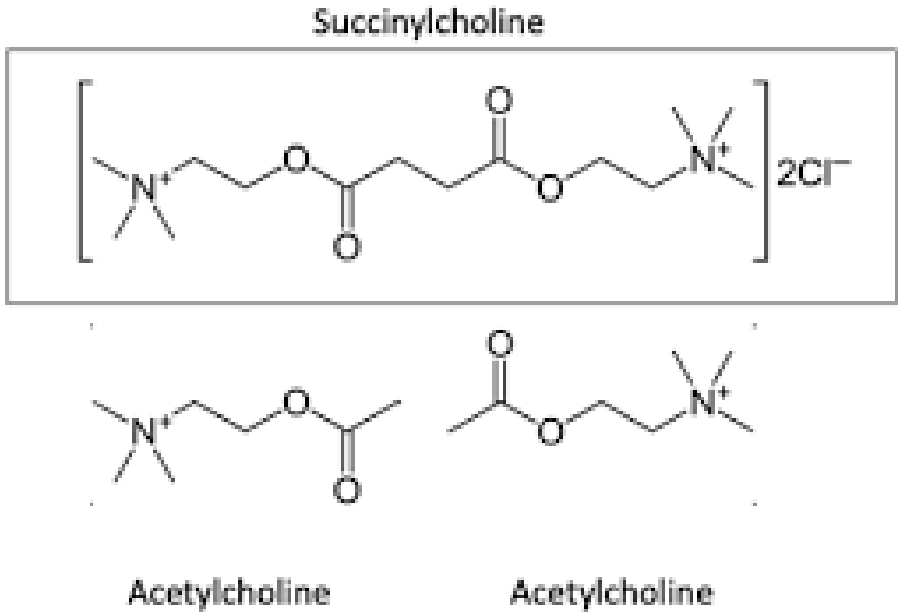


Depolarizing Neuromuscular Blocking Agent

Succinylcholine is a rapid onset and short-duration muscle relaxant administered by intravenous or intramuscular injection. The structure of succinylcholine is two acetylcholine molecules connected by a methyl group. The depolarization caused by succinylcholine results in momentary contractions of the muscles called **fasciculation** ; the patient's entire body may twitch and move for about 5 to 10 seconds. After the fasciculation, the succinylcholine remains attached to the receptor, and there is muscle paralysis for approximately 5 to 10 minutes..



❑ Adjuvant medications used in general anesthesia

The adjuvant medications are administered during the preoperative, intraoperative, and postoperative phase in support of balanced anesthesia. The chief adjuvant medications administered to support balanced anesthesia.

Drug	Pregnancy Category	Routes and Dosage Ranges	
		Adults	**Children**
(P) **Midazolam** (Nayzilam)	D	0.015–0.07 mg/kg IV PRN titrated to effect; usually given in 0.5–1-mg increments	0.25–1 mg/kg PO (15 mg max) 0.08–0.2 mg/kg IM 0.02–0.1 mg/kg IV in divided doses
(P) **Fentanyl** (Sublimaze, Abstral, Fentora, Ionsys; 🍁 Abstral, Duragesic, Fentora)	C	Balanced anesthesia: 2–8 mcg/kg with 50%–75% of total dose at induction Higher doses may be used for complex surgeries Sedation/analgesia: 25–50 mcg IV PRN titrated to effect	Balanced anesthesia: 1–3 mcg/kg standard range 4–10 mcg/kg higher range for complex surgeries
(P) **Dexmedetomidine** (Precedex; 🍁 Precedex)	C	Loading dose: 1 mcg/kg over 10 min Maintenance: 0.2–0.7 mcg/kg/h	Loading dose: 0.5–2 mcg/kg over 10 min Maintenance: 0.5–1 mcg/kg/h

❖ **Benzodiazepines**

Midazolam

The prototype drug, is a short-acting intravenous medication. Midazolam is the most common medication administered prior to surgery

❖ **Opioid Analgesics**

Fentanyl

synthetic opioid that is about 100 times more potent than morphine sulfate,

❖ **Alpha-2 Adrenergic Agonist**

Dexmedetomidine

is used to provide sedation for surgical, therapeutic, and diagnostic procedures and also as an adjunct to general anesthesia.


Thank
you