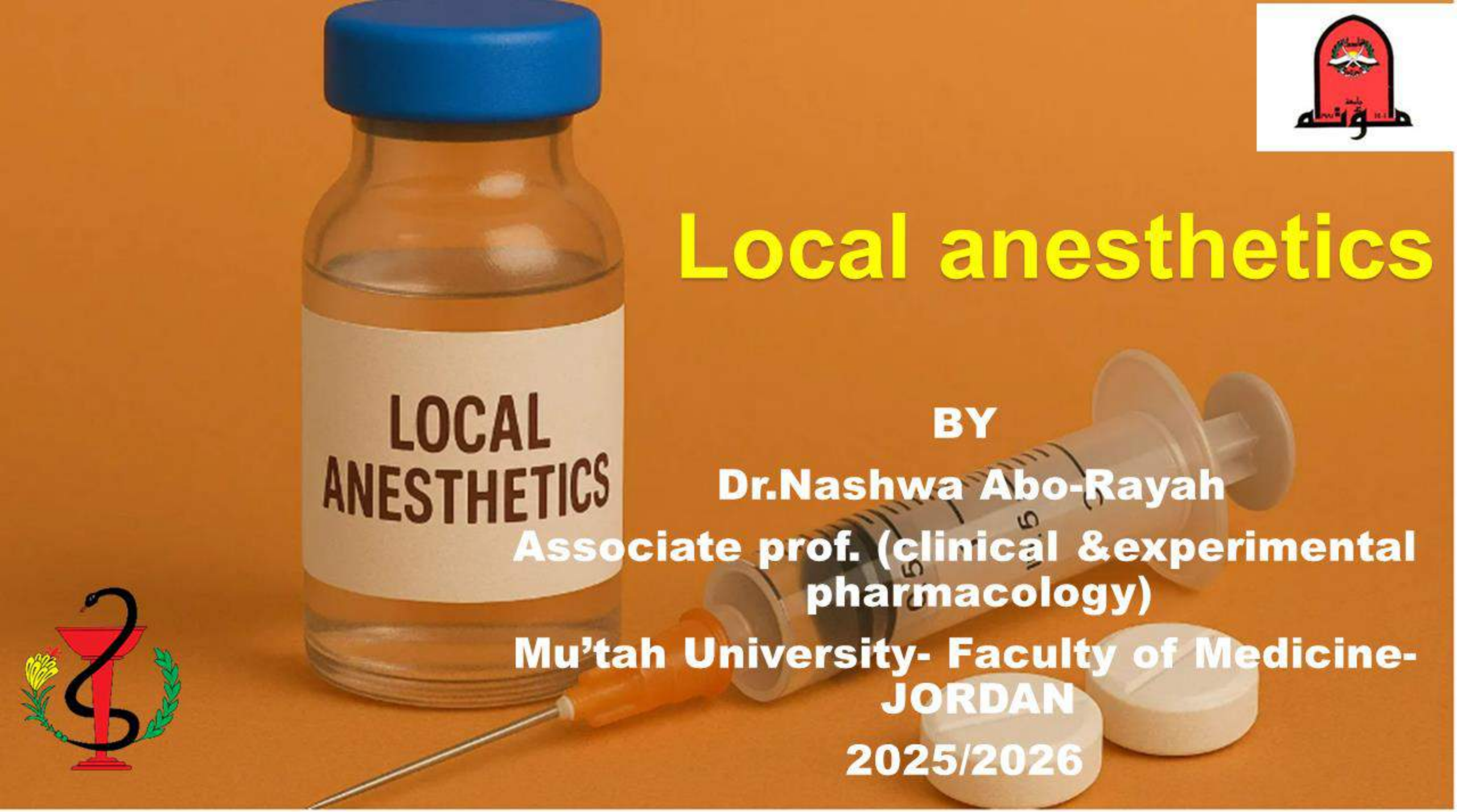

Local anesthetics

BY

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Objectives

- 1- Definition of local anesthesia
- 2- Types of nerve fibers affected by local anesthetics
- 3- Mechanism of action of local anesthetics
- 4- Factors affecting local anesthetic action
- 5- Ester and amide local anesthetics
- 6- Side effects of local anesthetics
- 7- Types of local anesthesia

What is a local anesthetic?

- A drug that **interrupt pain impulses** in a specific region of the body without loss of patient consciousness (patient remains fully awake and alert)
- Local anesthetic produces transient reversible **analgesia** in a circumscribed region of the body.

Indications of local anethesia

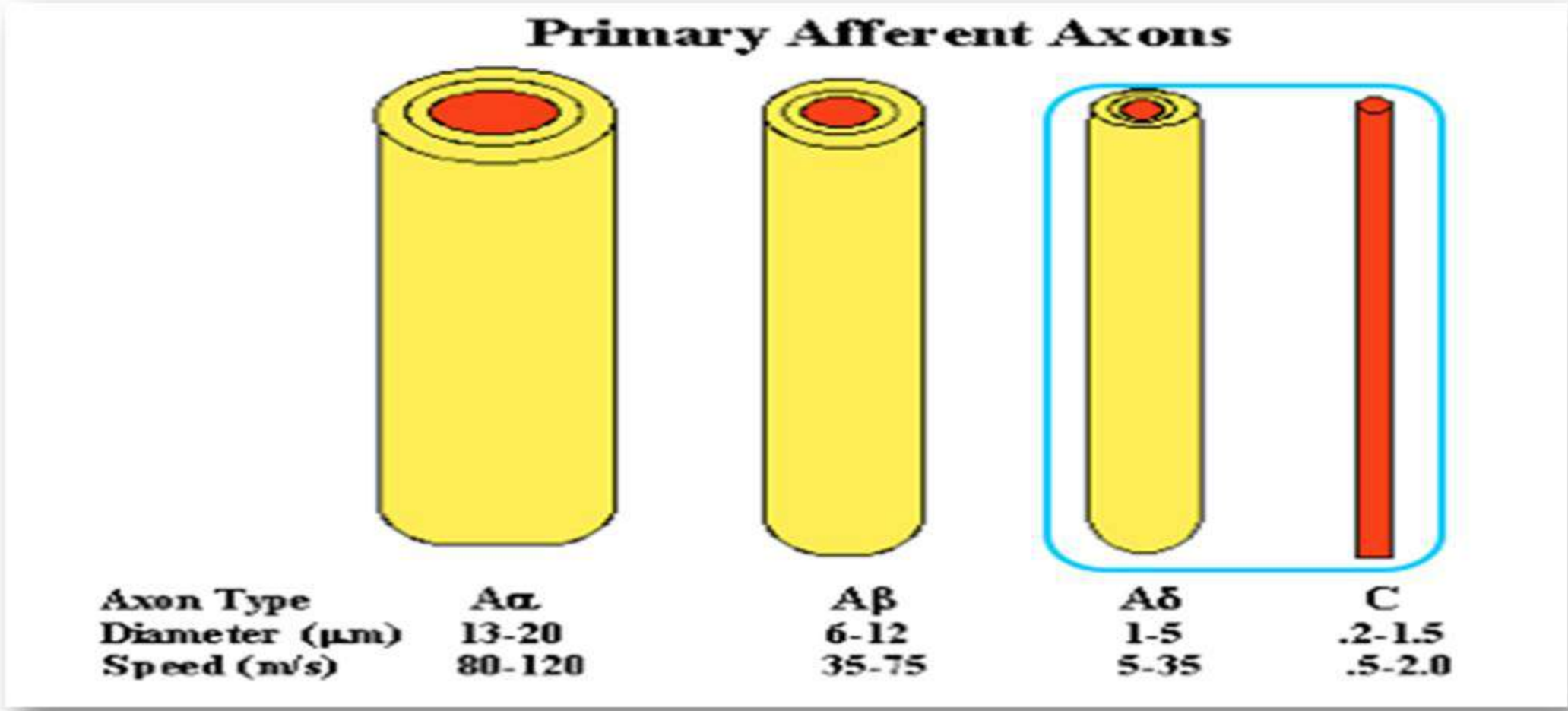
- **1- Minor surgeries**
- (e.g., biopsies, abcess removal ,dental procedures (fillings, extractions), suturing lacerations
- **2- Pain Management:** Localized pain relief for conditions like hemorrhoids, sore throats, or mouth ulcers, as well as postoperative pain management
- **3- When patients need to remain conscious during procedures:**
- Diagnostic Procedures: Lumbar puncture, joint aspiration, and bronchoscopy.

Nerve fibers affected by local anesthetics

- **Non-myelinated** and **smaller myelinated** fibers are easier to block than larger fibers.
- **Nerve fibers most affected by local anesthetics:**

- 1- Smaller non-myelinated C fibers (pain)
- 2- Small myelinated axons (Aδ sensory fibers)
- 3- B Fibers (Myelinated): Small, preganglionic autonomic fibers
- 4- A-ɣ and Aβ-Fibers (Myelinated): Medium diameter; responsible for proprioception and touch, respectively.
- 5- A-α Fibers (Myelinated): Largest, fastest; responsible for motor function and proprioception; least susceptible.

Types of nerve fibers



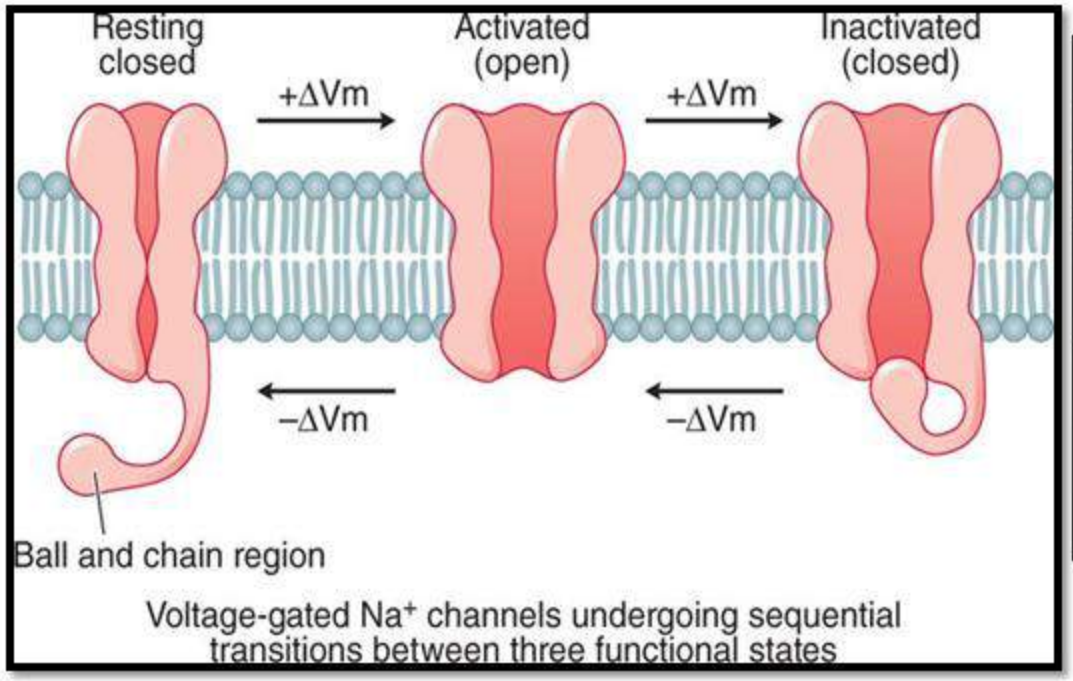
Order of blockade

- **Order of sensations**: Pain, temperature (Cold, Heat), proprioception (Touch, Deep pressure),
- **Order in nerve fibers**:
- Autonomic, Sensory, Motor
- **Anatomical Position**: In mixed nerve bundles, outer fibers are blocked before inner fibers.
- **Inflammation Effect**: Local anesthetics are less effective in inflamed tissue
- **Recovery from local anesthesia** typically occurs **in the reverse order of onset**, as the concentration of the drug at the nerve site decreases.
- **Motor** function returns first, followed by **proprioception, touch**, and **finally, pain/temperature** sensations. The last areas to be blocked (e.g., motor) are the first to recover.

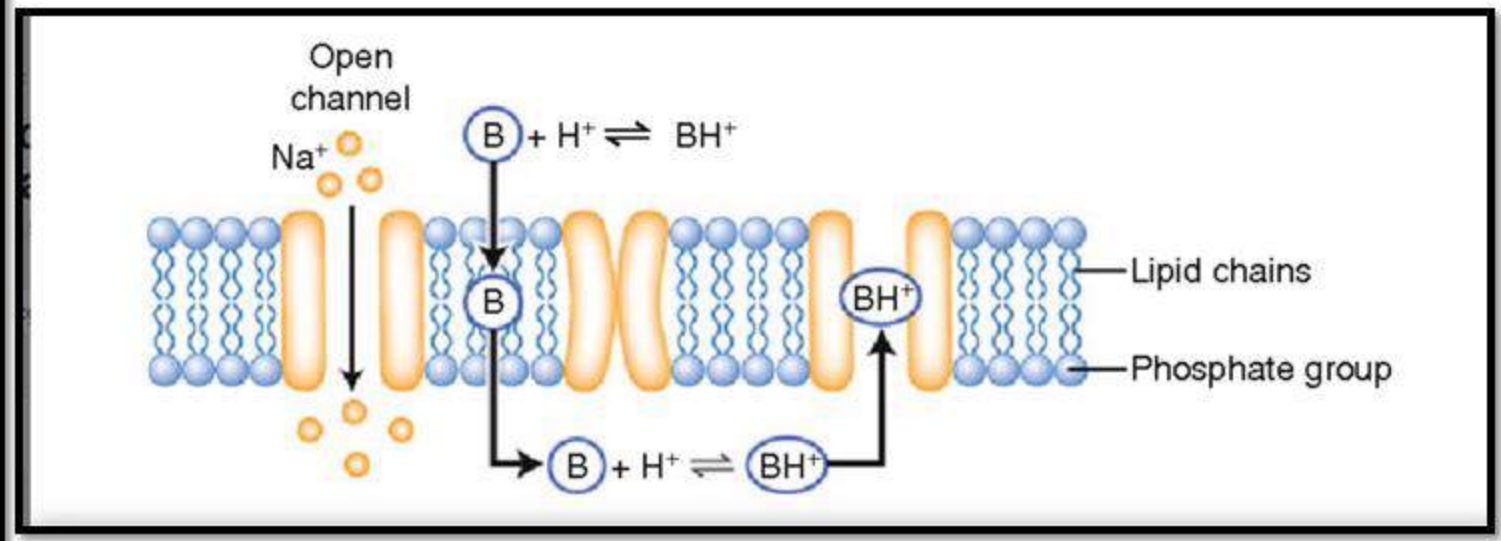
Mechanism of action

- **Lipophilic**, **unionized** local anesthetic molecules cross the phospholipid neuronal membrane.
- The molecules dissociate to ionized and un-ionized molecules, depending on the intracellular pH and the pKa of the local anesthetic.
- The ionized form binds to open voltage-gated Na+ channels in a **reversible** and **concentration-dependent manner**.
- The binding site for local anesthetics is only accessible when the channel is open.
- Bound local anesthetic drug stabilizes the inactivated state, preventing further neuronal transmission.
- With increased concentrations of local anesthetic inhibit all nerve conduction.

Mechanism of action of LA



Voltage-gated Na^+ channels undergoing sequential transitions between three functional states



Local anesthetic binds to the inner membrane in a cationic form and physically blogging Na channel.

N.B. inside of the neuron is slightly acidic

Factors affecting local anesthesia action

1. Lipid solubility: a lipophilic local anesthetic is more potent because it is easier to cross nerve membranes (penetration, potency, onset of action)

2. Protein binding:

- Local anesthetics with high protein binding to α1-acid glycoprotein have a longer duration of action.
- Hypoxia, hypercarbia, and acidaemia all decrease protein binding, and increase the risk of toxicity.
- Children younger than 6 months have less protein binding capacity.

Factors affecting local anesthesia action

3. **pKa:**

-The pKa is the pH at which 50% of the local anesthetic is in the ionized form and 50% is in the unionized form.

All local anesthetics are weak bases with pKa = 8-9:

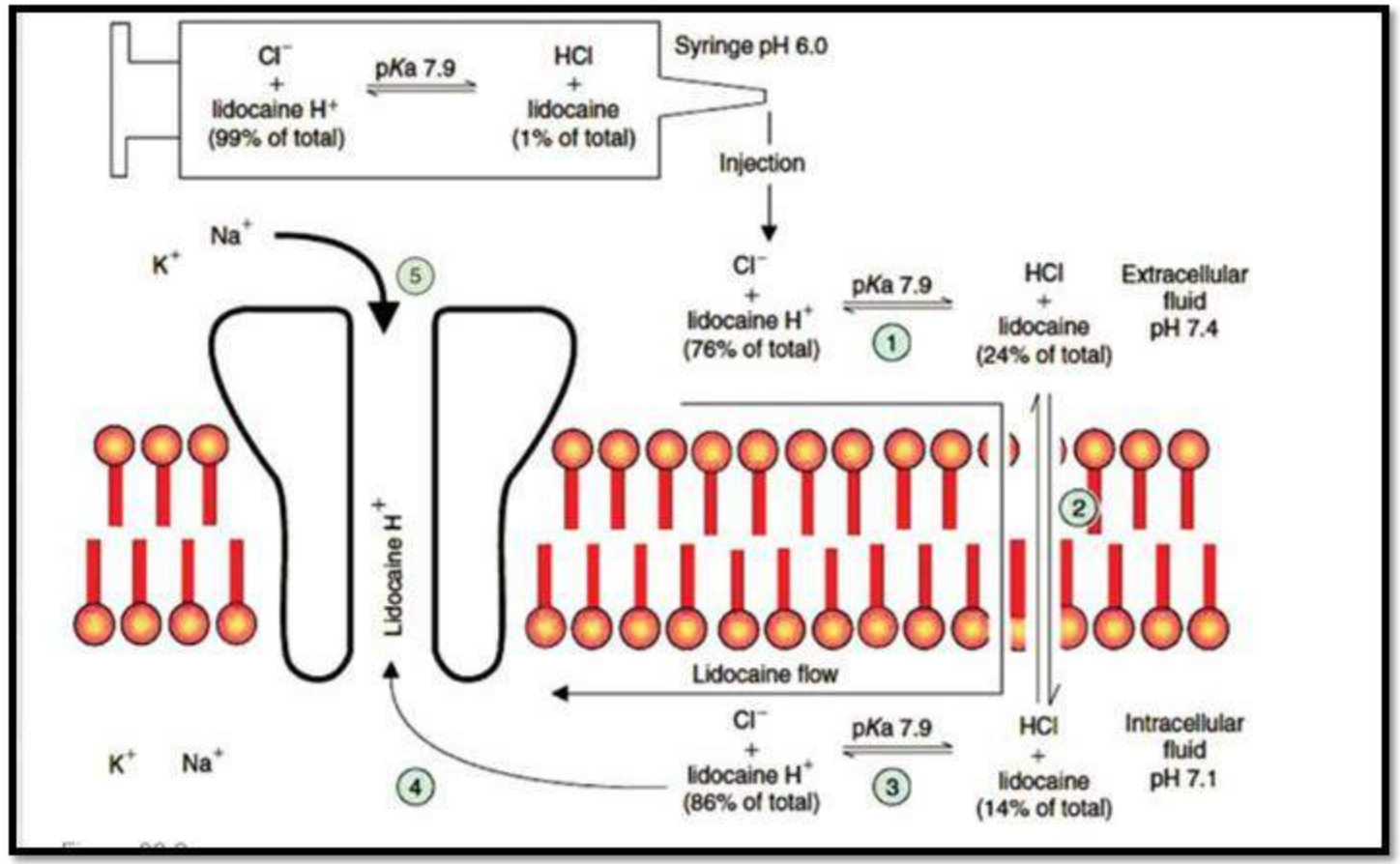
- Local anesthetics with pKa close to **physiologic pH** are associated with a greater fraction of the molecules existing in the unionized form = more penetration across nerve membranes = faster onset. (Small gap between pH and pKa)
- Local infection (**acidosis: 6.4**) increases the ionized drug fraction which means less drug will be available to penetrate across membranes and bind to intracellular local anesthetic receptors on Na+ channels = slower onset.(Increased gap between pH and pKa). (**formulation with sodium bicarbonate**)

4. **Dose:** Increasing dose of the anesthetic will increase the duration of the block (**and adverse effects**).

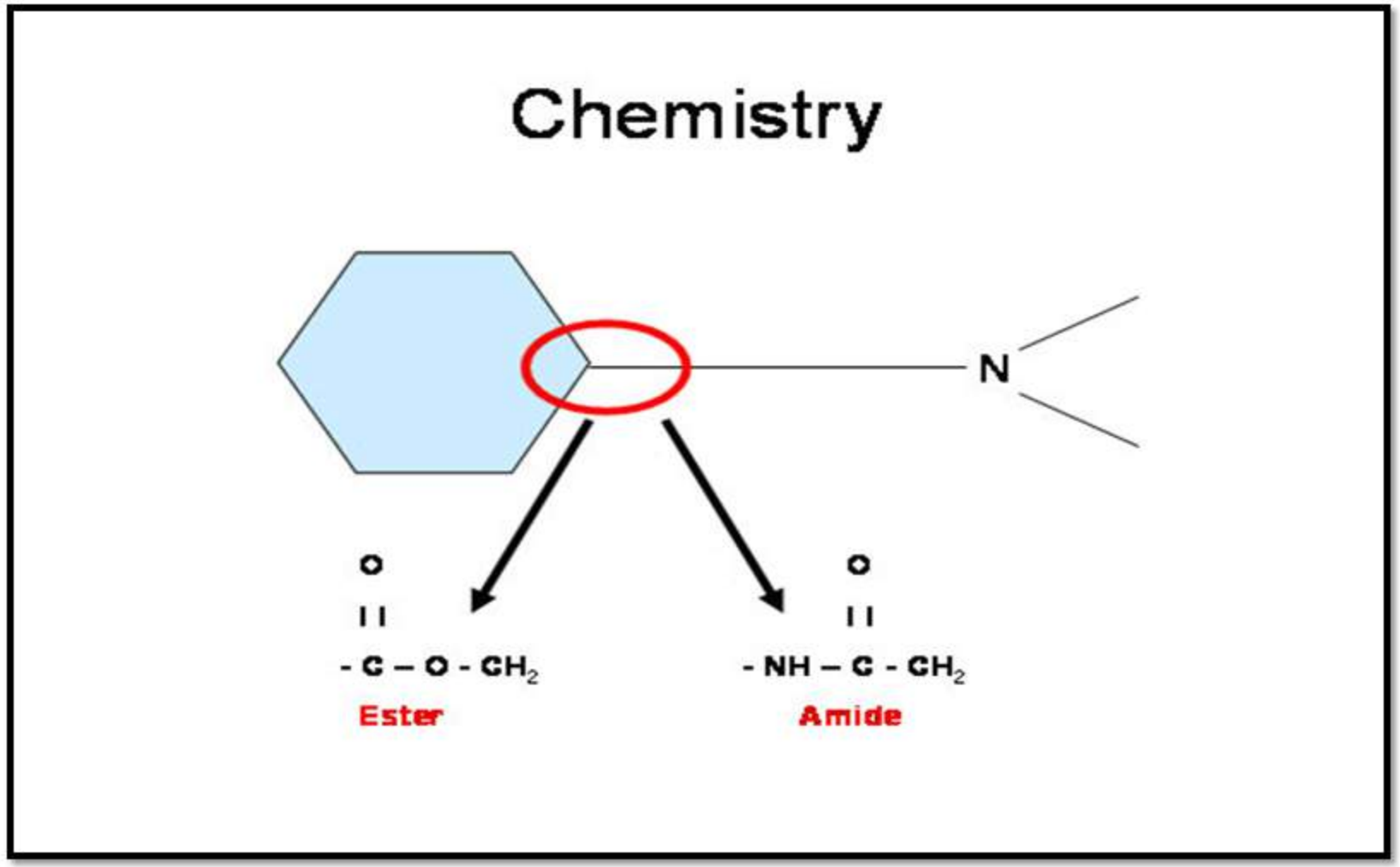
5. Molecular weight

- The smaller the molecular weight, the more rapidly molecules diffuse through membranes.

Pka of local anesthetic



Chemical structure of local anesthetic drugs



	Esters	Amides
Chemistry	Have an ester (-COO-) link (easy degradation) between the aromatic group and the amino terminal	Has an amide (-NHCO-) link (stable, long duration, widely used) between the aromatic group and the amino terminal.
Examples	**Cocaine:** natural: not used: all LA named after it. **Procaine**: prototype: short acting: many side effects, less potent, rarely used. **Tetracaine**: long acting **Benzocaine:** Topical gel or ointment **surface anesthesia only** due to its **toxicity.**	**Lidocaine (lignocaine)** : prototype: has fast onset, commonly-used (topical, injection). **Antiarrhythmic** **Bupivacaine & Ropivacaine**: **long duration** (long procedures: obstetrics (spinal anesthesia), **safe** (less cardio toxic) **Prilocaine: only surface anesthesia**: if reach systemic circulation can produce metHb (never in CS: metHB in fetus) **Articaine: common use in dentistry**: ester and amide bonds: short duration: 30 min.
t1/2	Few minutes	Few hours
Metabolism	**By plasma pseudocholinestrase**. ❑ P-aminobenzoic acid is a metabolite & a common cause allergy.	**By the liver.**
Incidence of allergic Reactions	High (cross allergy between esters).	Rare

Local adverse effects

- **Local:**
- Irritation and inflammation at the site of administration
- Vasodilatation: bleeding
- **local ischemia** may arise from a co-administered vasoconstrictor, therefore this should be avoided in the extremities such as the digits.
- **Local anesthetic reversal:**
- Persistent numbness, drooling and inability to eat after local anesthesia for dental surgery are unpleasant.
- **Phentolamine mesylate** is a non-selective alpha-adrenergic blocker that causes vasodilation.
- This increases the blood flow and is reported to halve the reversal time of local anesthesia.

Systemic adverse effects

Systemic (high doses can reach systemic circulation)

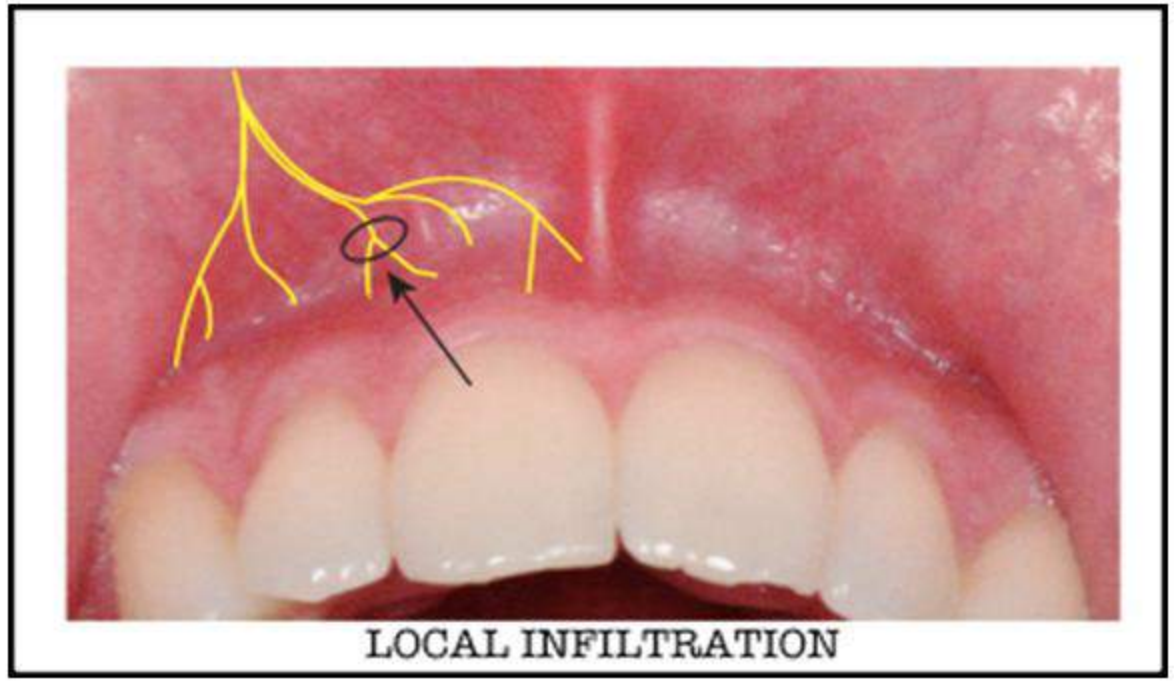
- **1- CVS:** bradycardia and hypotension
- **2- CNS**: dizziness, confusion and restlessness
- **3-Allergy** is rare but can occur with ester group
- **4- placental transfer**: The rate and degree of diffusion of local anesthetic across the placenta depends on **protein binding**, **pKa**, and **maternal and fetal pH**.
- In prolonged labor, acidosis in the fetus can result in accumulation of local anesthetic in the fetus by ion trapping.
- However, because of rapid hydrolysis, ester local anesthetics do not cross the placenta in significant amounts.
- **Spinal anesthesia**:
- **1- Injury of spinal cord**: spinal shock (fatal), paralysis: most dangerous
- **2- Headache** due to leakage of CSF: most common
- **3- Contamination**: risk of septic meningitis

Types of local anesthesia

- Infiltration anesthesia
- Regional anesthesia
- Surface anesthesia

Infiltration anesthesia

- Administration of the local anesthetic solution **intradermal (ID)**, **subcutaneously (SC),** or **submucosal** **across the nerve path** that supplies the area of the body that requires anesthesia.



LOCAL INFILTRATION

Topical (surface) anesthesia

- Superficial loss of sensation in conjunctiva, mucous membranes, or skin, produced by direct application of local anesthetic **solutions, ointments, gels or sprays.**

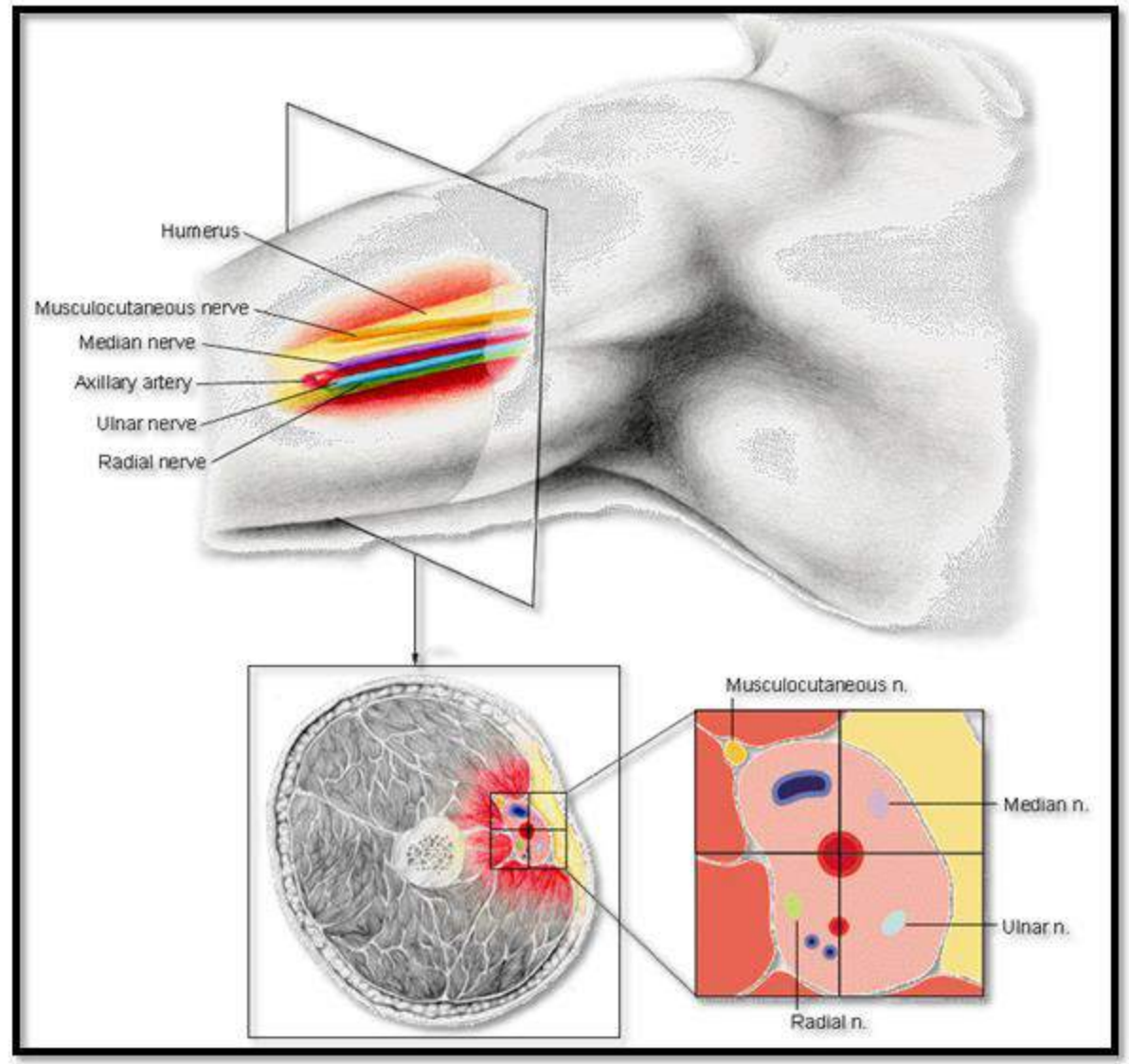
Regional anesthesia

- Nerve block
- Intravenous
- Epidural
- Intrathecal (spinal anesthesia)

Nerve block

- Inject a drug around the nerve

- Anaesthetize a region
- **Example:**
- brachial plexus block for arm/shoulder surgery



Intravenous local anesthesia

- **The Bier block**: **intravenous local anesthesia (IVLA)**
- Safe, effective, and cost-efficient way to provide short-term anesthesia and analgesia during surgery on an extremity.
- This technique requires minimal additional equipment and can be performed in a variety of clinical environments.

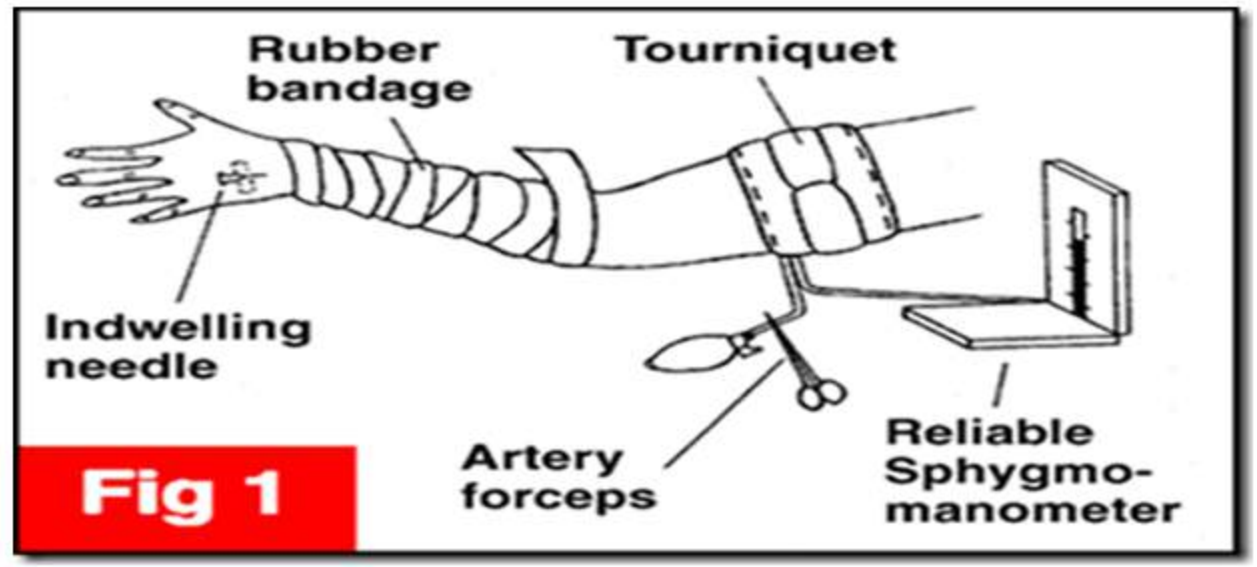
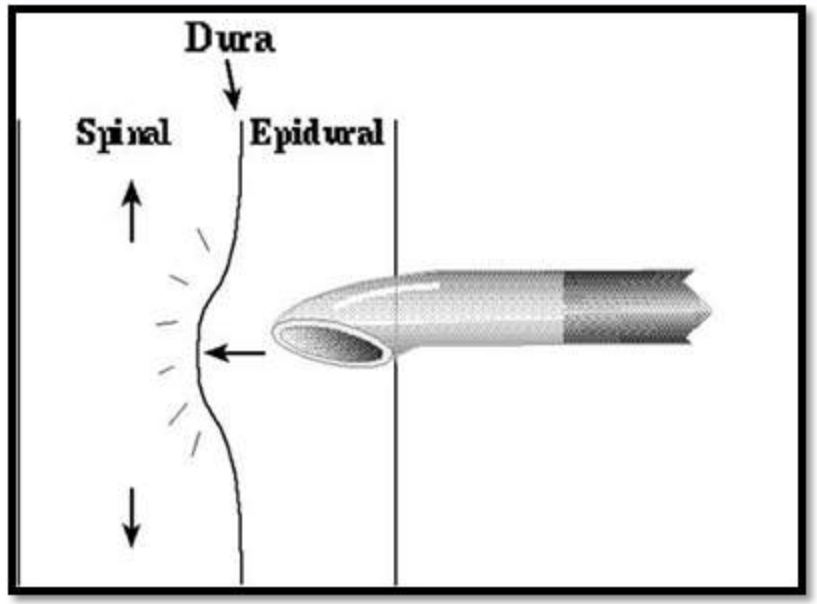
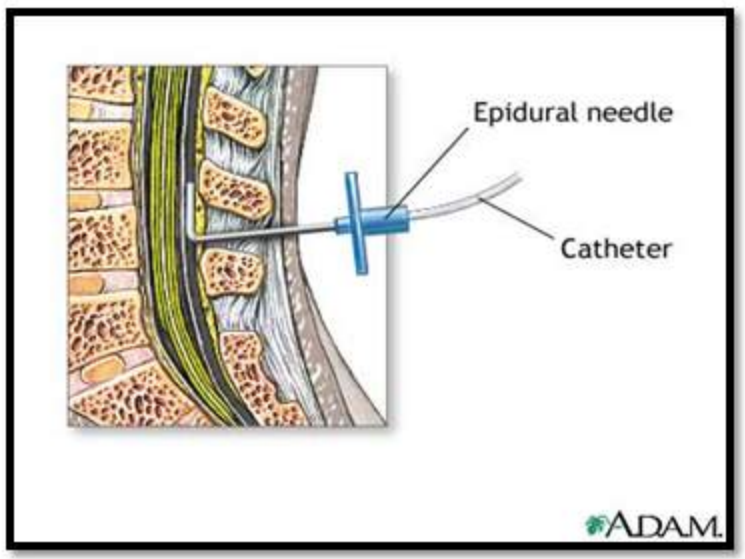


Fig 1

Extradural/epidural

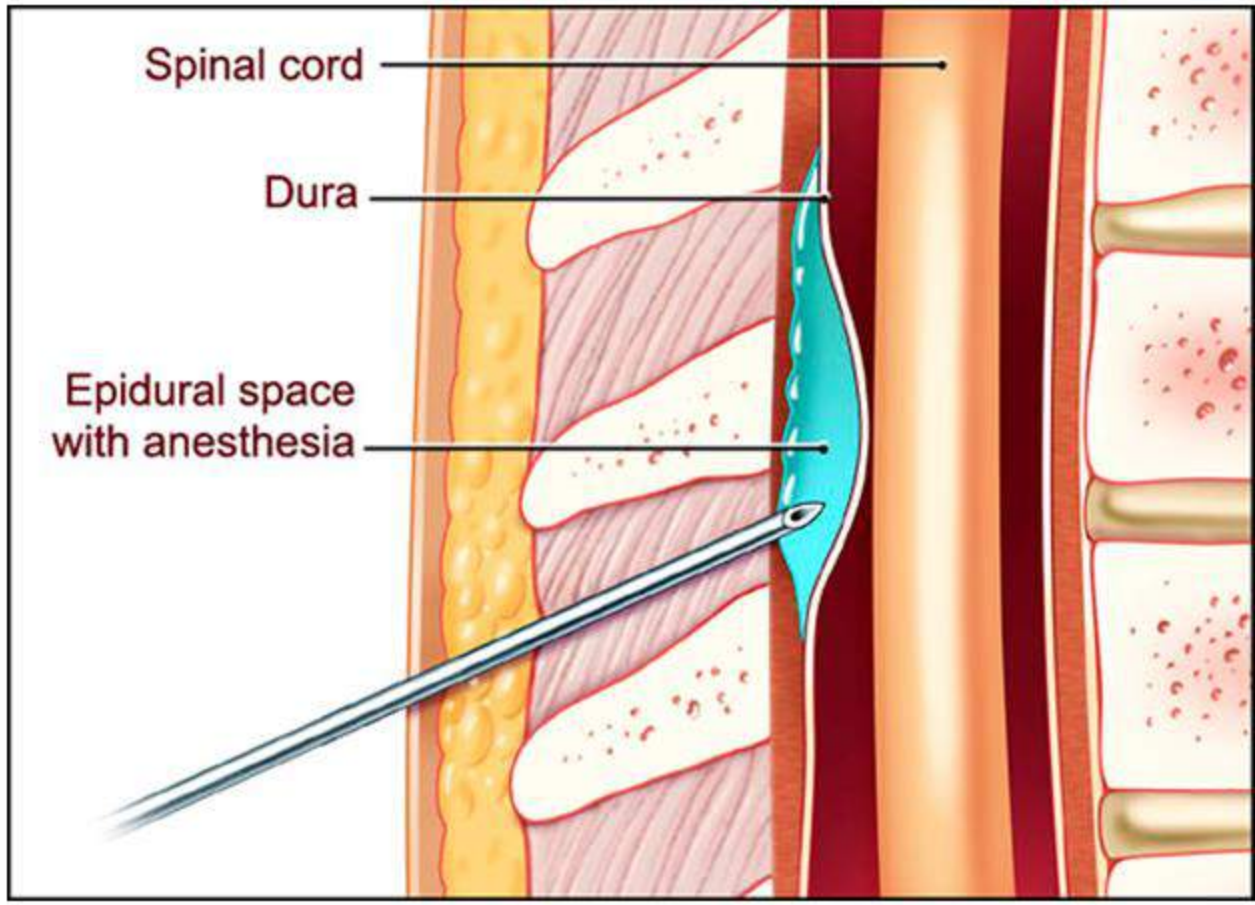
- Thoracic, lumbar, sacral
- Act on **nerve roots**
- **Advantages**:
- 1- No hypotension
- 2- Longer duration than spinal anesthesia
- 3- Ability for catheter insertion for drug administration e.g. morphine in terminal cancer cases





Spinal anesthesia (subdural, subarachnoid)

- **Block nerve roots of cuada equine**: anesthesia and analgesia of lower half of the body.
- Between L3 and L4(to avoid spinal cord injury)
- Duration of action: 1-1.5 hrs.
- **<u>Disadvantages:</u>**
- 1- Hypotension
- 2- Spinal cord injury
- 3- Septic meningitis



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Thank you