Local anesthetics
PNS module

BY

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2023/2024

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

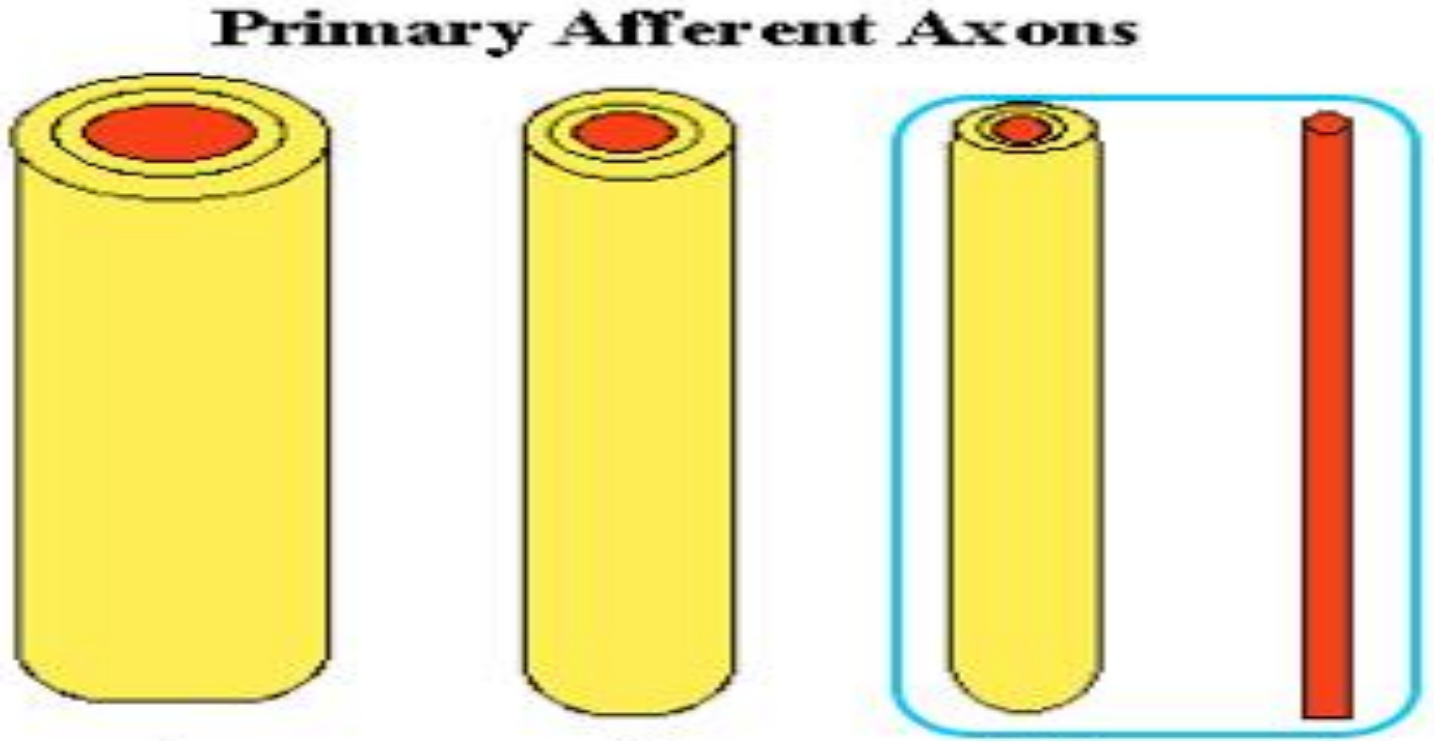
What is a local anesthetic?

- A drug that interrupt pain impulses in a specific region of the body without loss of patient consciousness.
- Local anesthetic produces transient reversible analgesia in a circumscribed region of the body.

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:**
- Smaller non-myelinated C fibers (pain)
- small myelinated axons (Aδ sensory fibers)

Types of nerve fibers

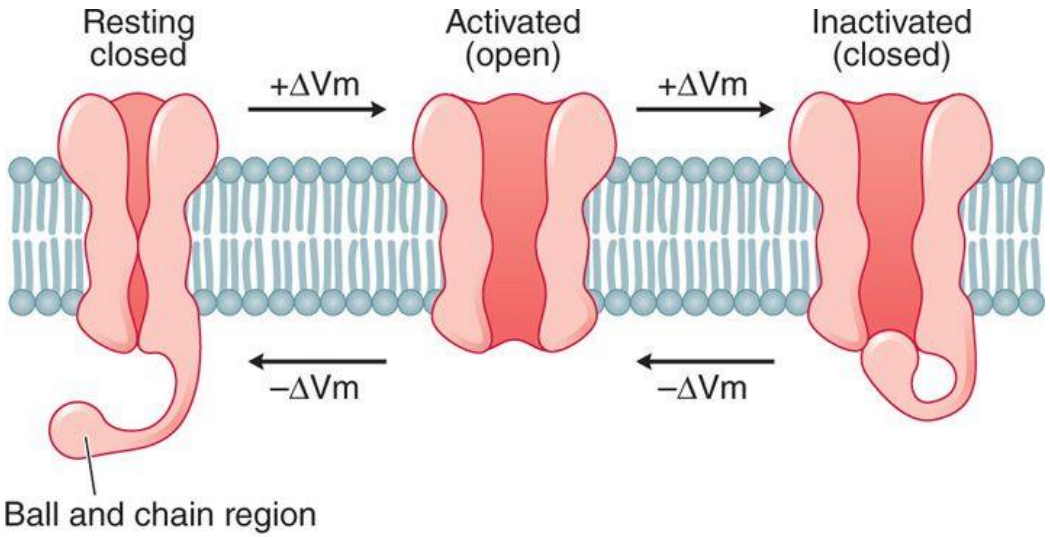


Axon Type	Aα	Aβ	Aδ	C
Diameter (μm)	13-20	6-12	1-5	.2-1.5
Speed (m/s)	80-120	35-75	5-35	.5-2.0

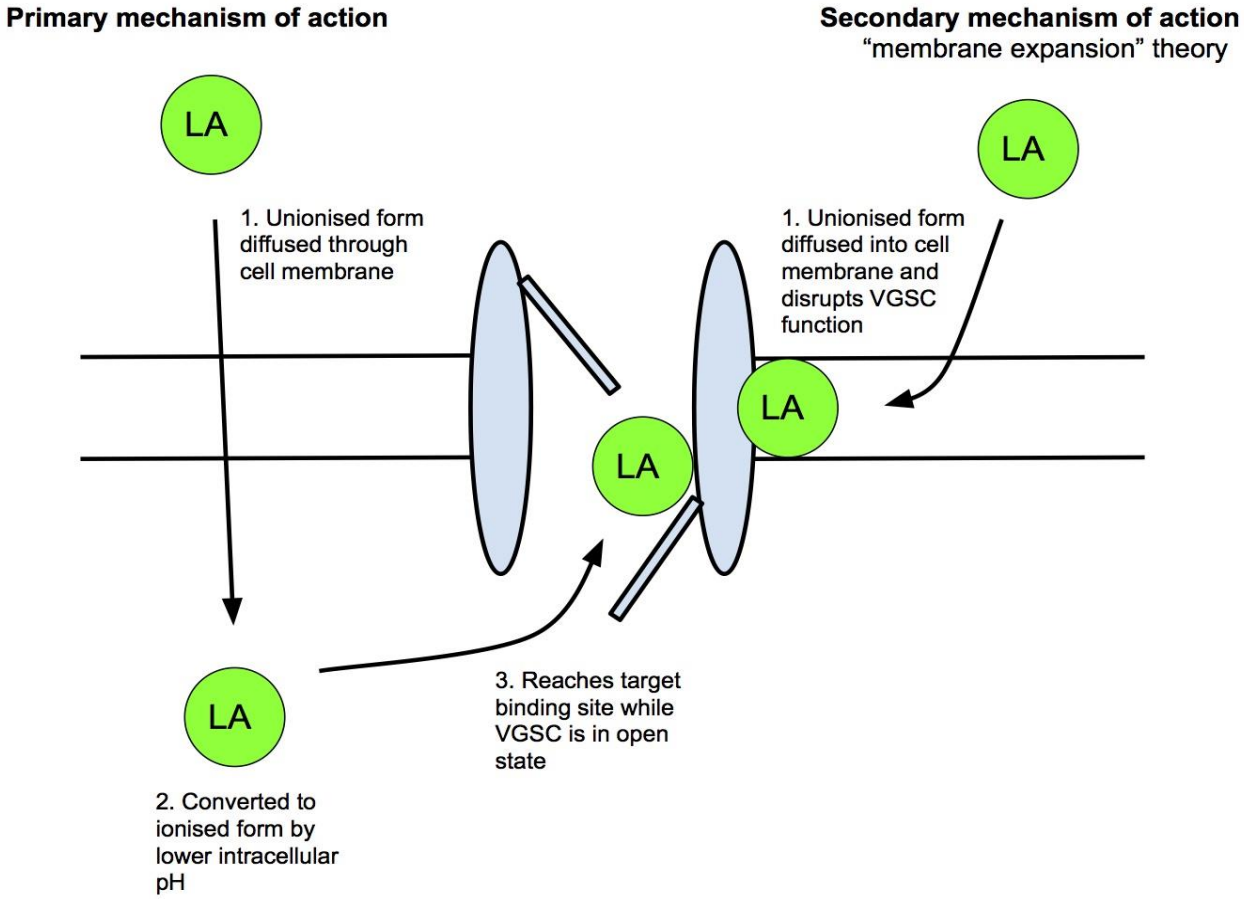
Order of loss of sensations

- Pain
- Cold
- Heat
- Touch
- Deep pressure

- **<u>Order in nerve fibers</u>**:
- Autonomic
- Sensory
- Motor



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

Mechanism of action of local anesthetics

- **They block nerve conduction:**

1. By interacting directly with specific site on neuronal Na+ channels (active Na channels), inhibiting Na+ ion influx.

2. By impairing both generation and propagation of the action potential in the axons

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 a higher degree of protein binding have a prolonged duration of action (duration of action)

3. **pKa:**

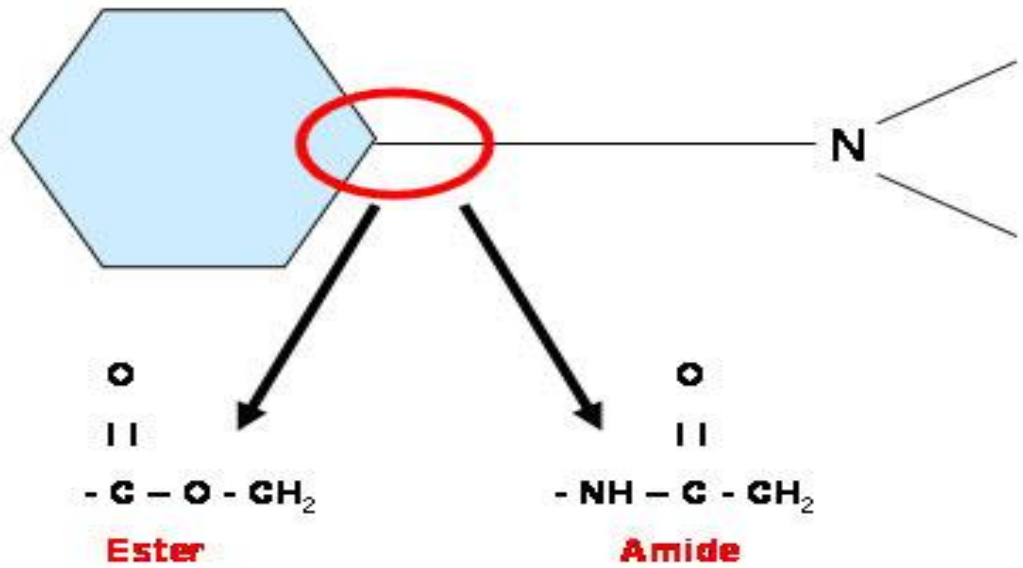
-The pKa is the pH at which 50% of the local anesthetic is in the ionized form and 50% is in the unionized form.

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 (**side effects**).

Chemistry



	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	**Procaine: prototype:** short acting: many side effects, less potent, rarely used. **Cocaine**: natural: not 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) **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**

Side effects

- **Local:**
- Irritation and inflammation at the site of administration
- Vasodilatation:
- but local ischemia may arise from a co-administered vasoconstrictor, therefore this should be avoided in the extremities such as the digits.

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

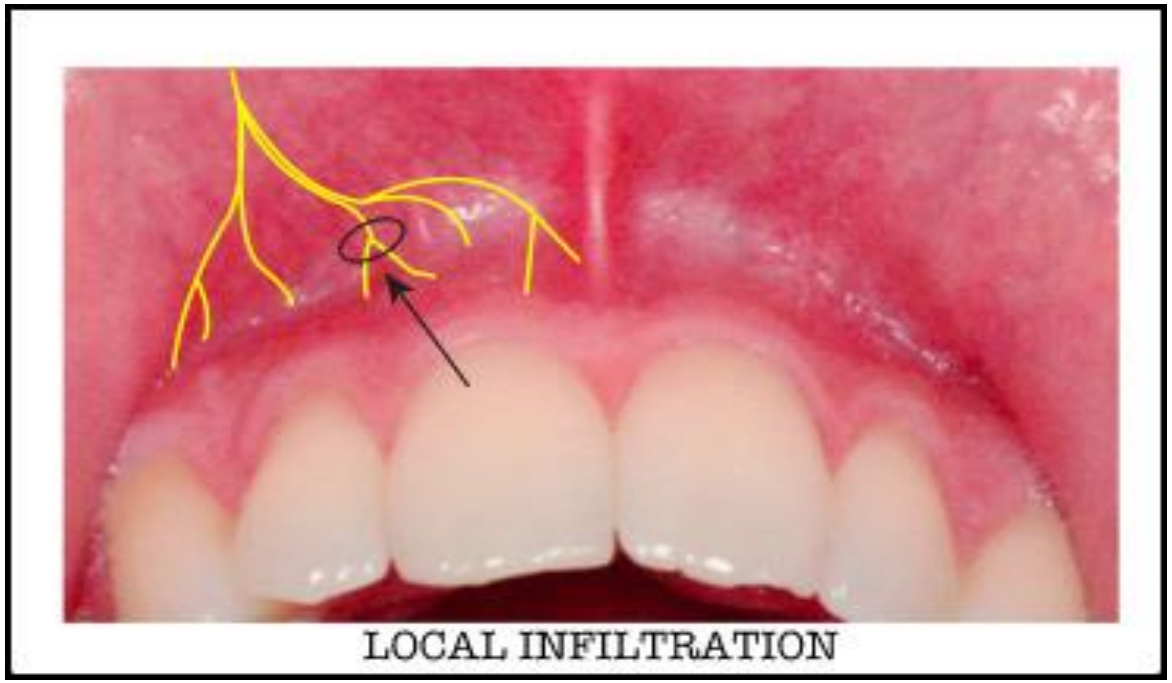
- **Spinal anesthesia**:
- 1- Injury of spinal cord: spinal shock (fatal), paralysis: most dangerous
- 2- Headache due to leakage of CSF: most common
- 3- Contamination: risk of septic meningitis

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.



Topical (surface) anesthesia

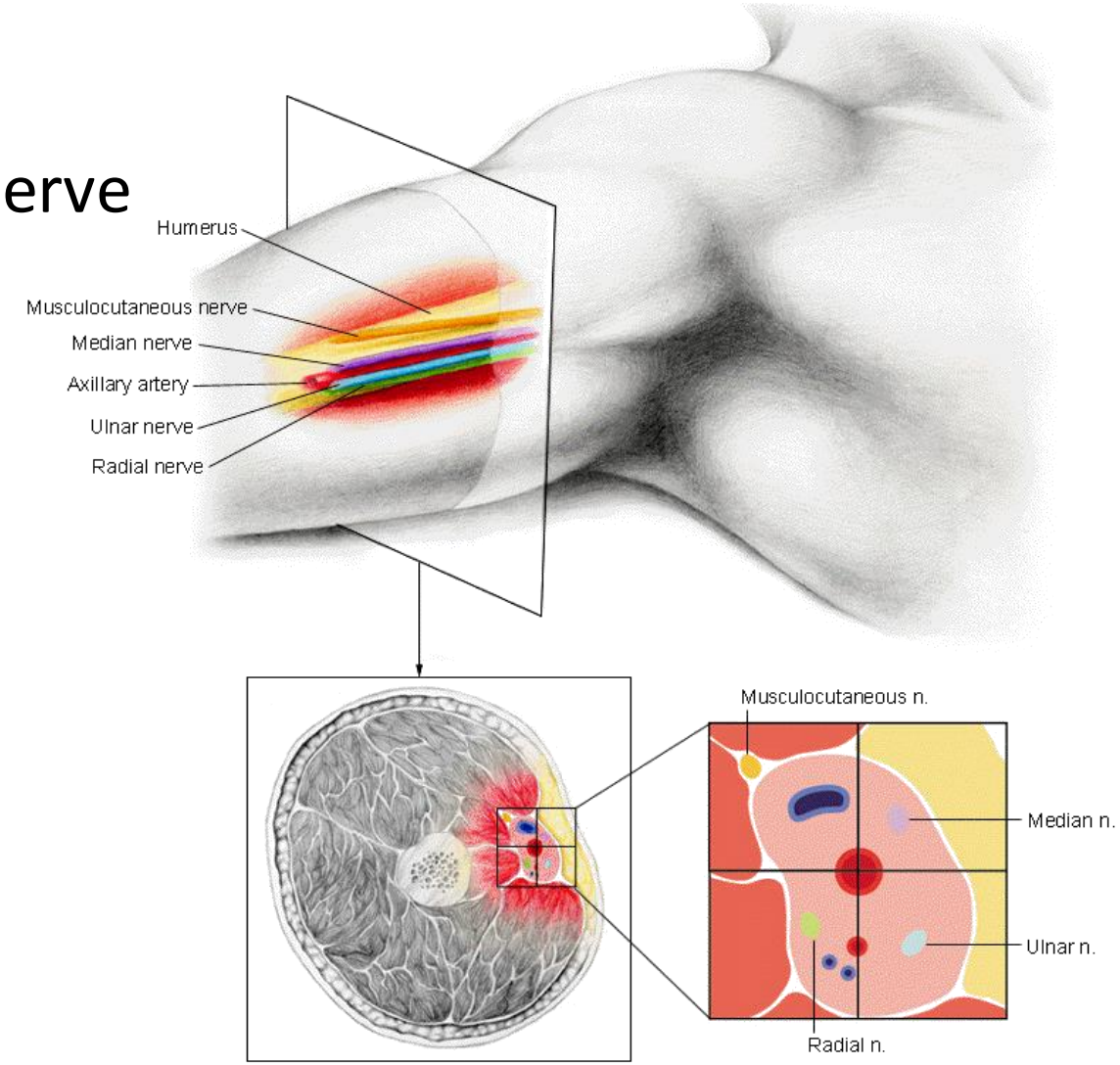
- Superficial loss of sensation in conjunctiva, mucous membranes, or skin, produced by direct application of local anesthetic solutions, ointments, gels or sprays.

Regional anesthesia

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

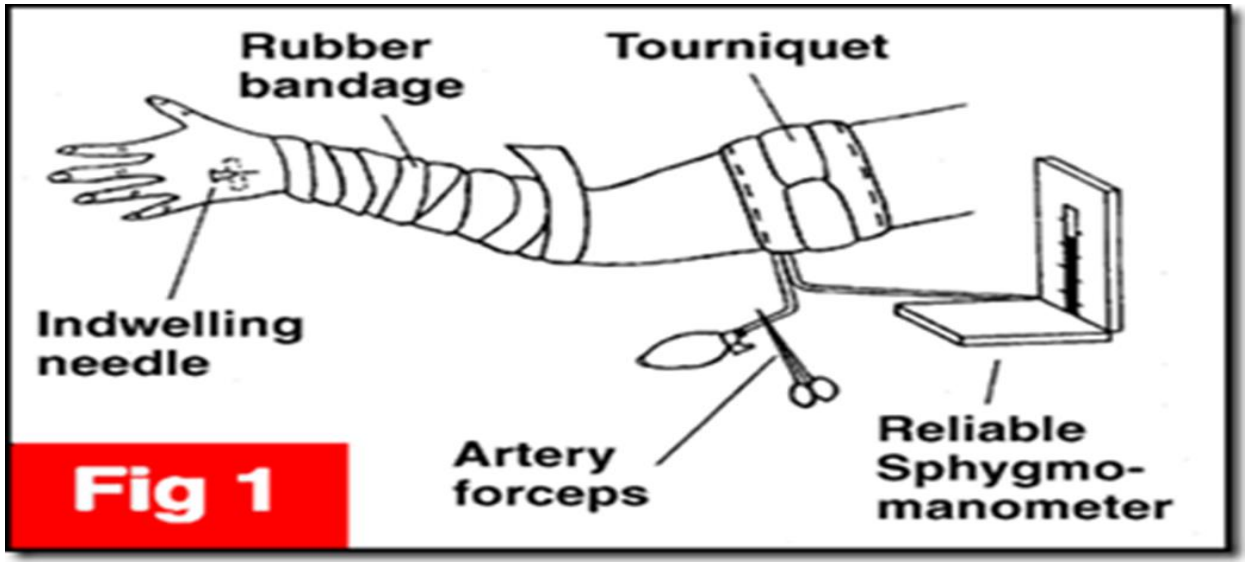
Nerve block

- Inject a drug around the nerve
- Anaesthetize a region



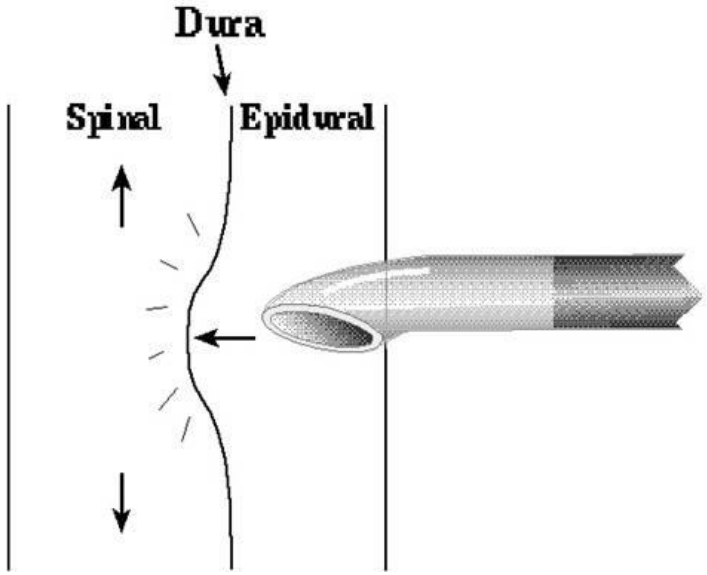
Intravenous local anesthesia

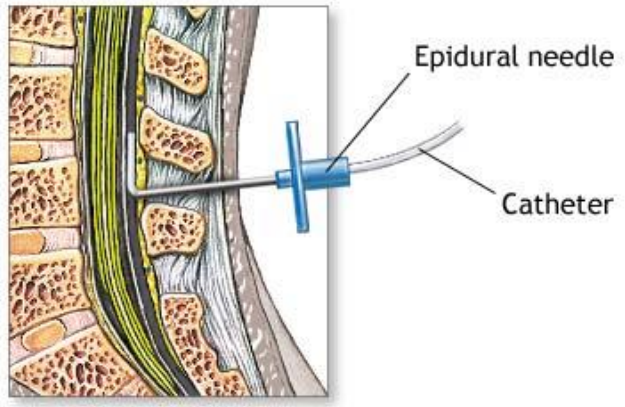
- **The Bier block**: intravenous local anesthesia (IVLA)
- Safe, effective, and cost-efficient way to provide short-term anesthesia and analgesia during surgery on an extremity.
- This technique requires minimal additional equipment and can be performed in a variety of clinical environments.



Extradural/epidural

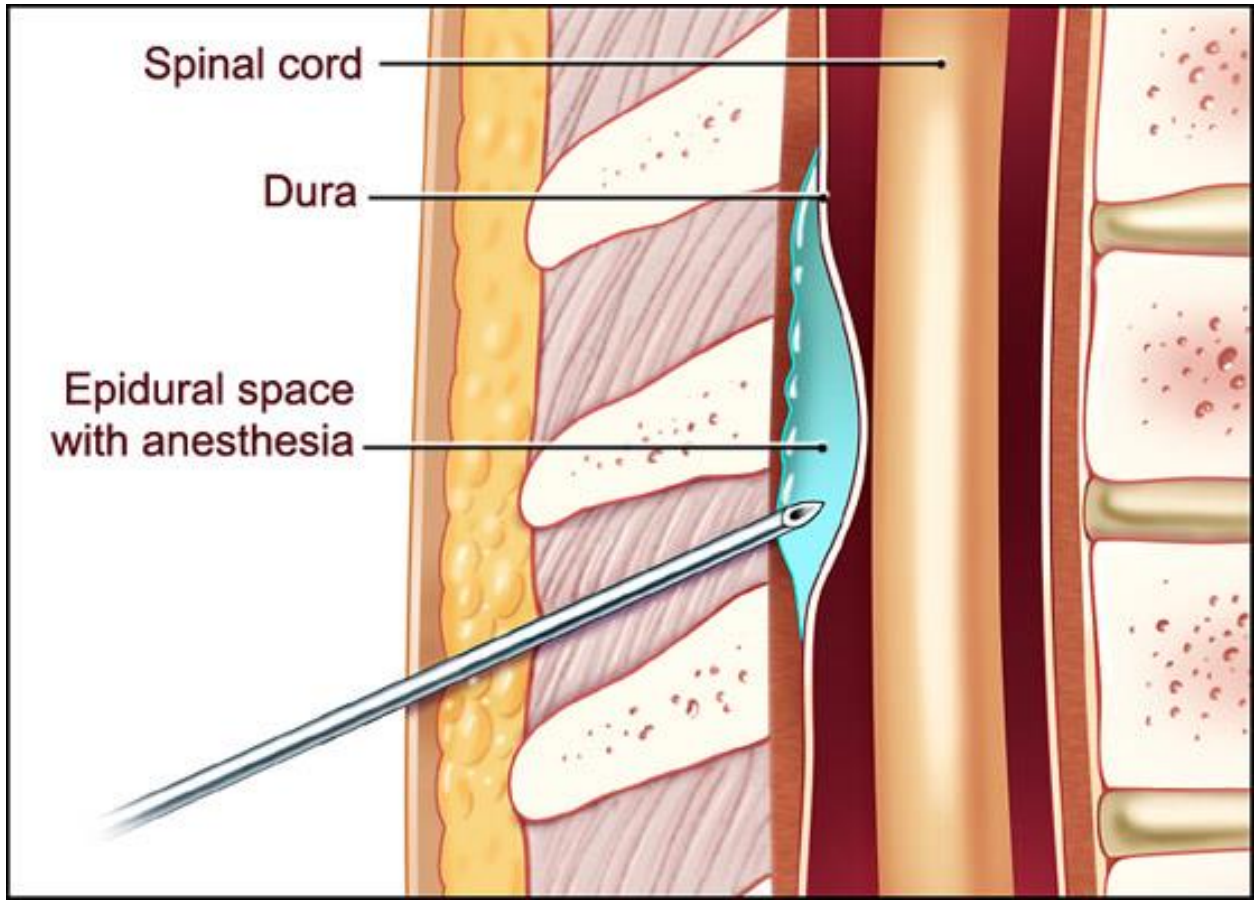
- Thoracic, lumbar, sacral
- Act on nerve roots
- **<u>Advantages</u>**:
- 1- No hypotension
- 2- Longer duration than spinal anesthesia
- 3- Ability for catheter insertion for drug administration





Spinal anesthesia (subdural, subarachnoid)

- Block nerve roots of cuada equina
- Between L3 and L4
- **Disadvantages:**
- 1- Hypotension
- 2- Spinal cord injury
- 3- Septic meningitis



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Thank you