# LOCAL ANAESTHETICS

# LEARNING OBJECTIVES

***After this session you should be able to:***

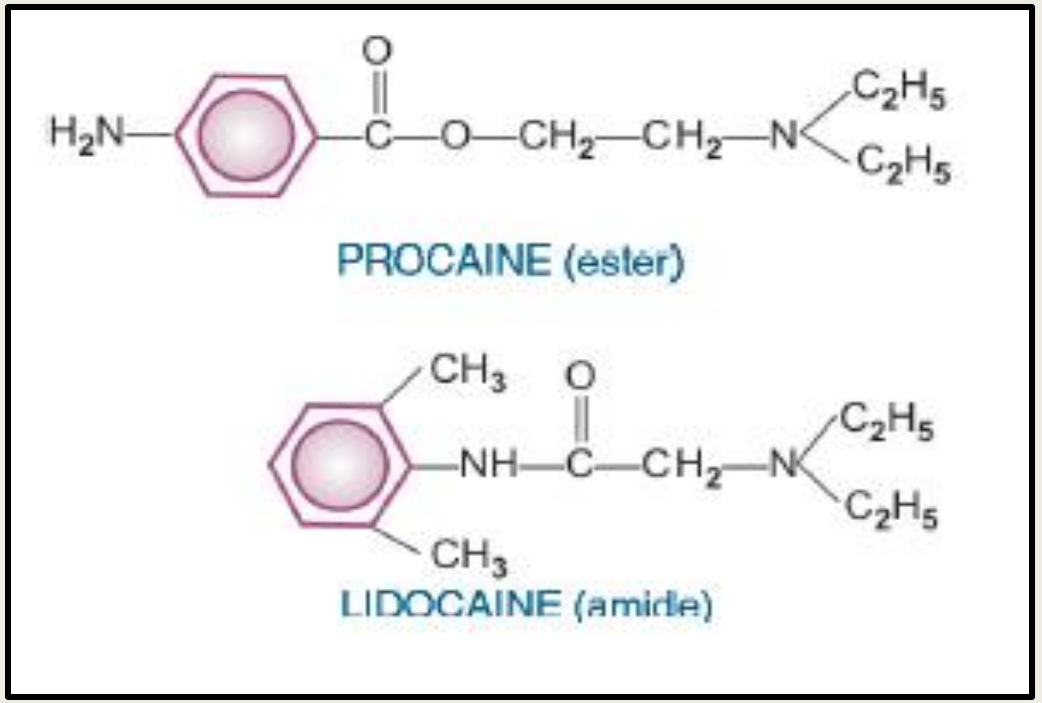
- **define local anesthesia;**
- **classify local anesthetics;**
- **describe pharmacokinetic properties of commonly used local anesthetics;**
- **describe their mechanism of action;**
- **comprehend the structure-activity characteristics of local anesthetics; and**
- **describe the toxicity of local anesthetics.**

# CLASSIFICATION

## ACCORDING TO CHEMISTRY

- ESTERS
- Cocaine
- Procaine
- Tetracaine
- Benzocaine

- AMIDES
- Lidocaine
- Mepivacaine
- Bupivacaine
- Ropivacaine
- Articaine

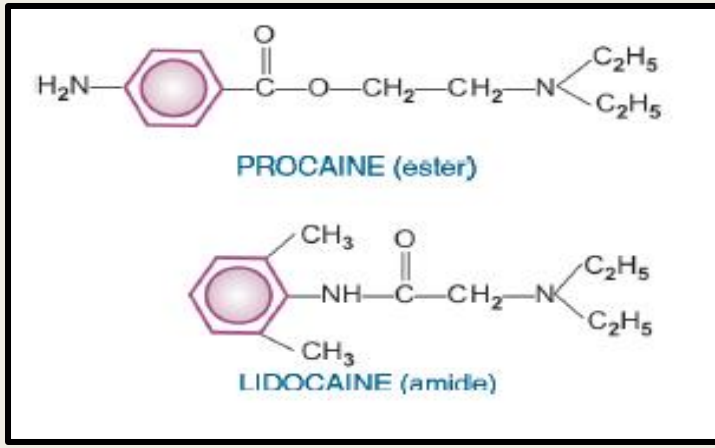


# CLASSIFICATION

- **Injectabe anaesthetics**
- **Short duration:**
  - Procaine
  - Chloroprocaine
- **Intermediate duration:**
  - Lidocaine
  - Prilocaine
- **Long duration:**
  - Bupivacaine
  - Ropivacaine
  - Tetracaine

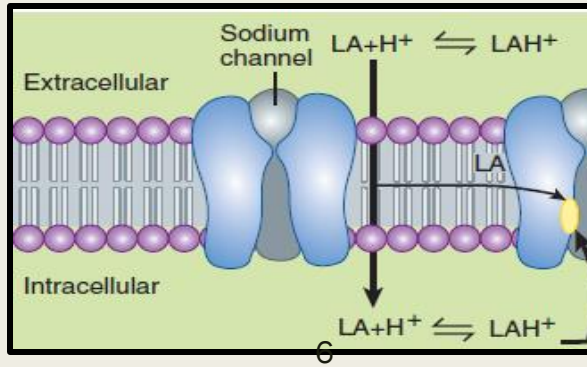
- **Surface anaesthetics**
- Cocaine
- Benzocaine
- Lidocaine
- Tetracaine

# LOCAL ANAESTHETICS




- Weak bases
- **Two components:**
  - Hydrophilic : Tertiary amine: Ionisable
  - Lipophilic: Aromatic ring
  - Alkyl chain (Ester or amide)
- Absorption of local anaesthetics(Handerson Hasselbalch equation)
  - pKa=Ph-log[base]/[conjugate acid]

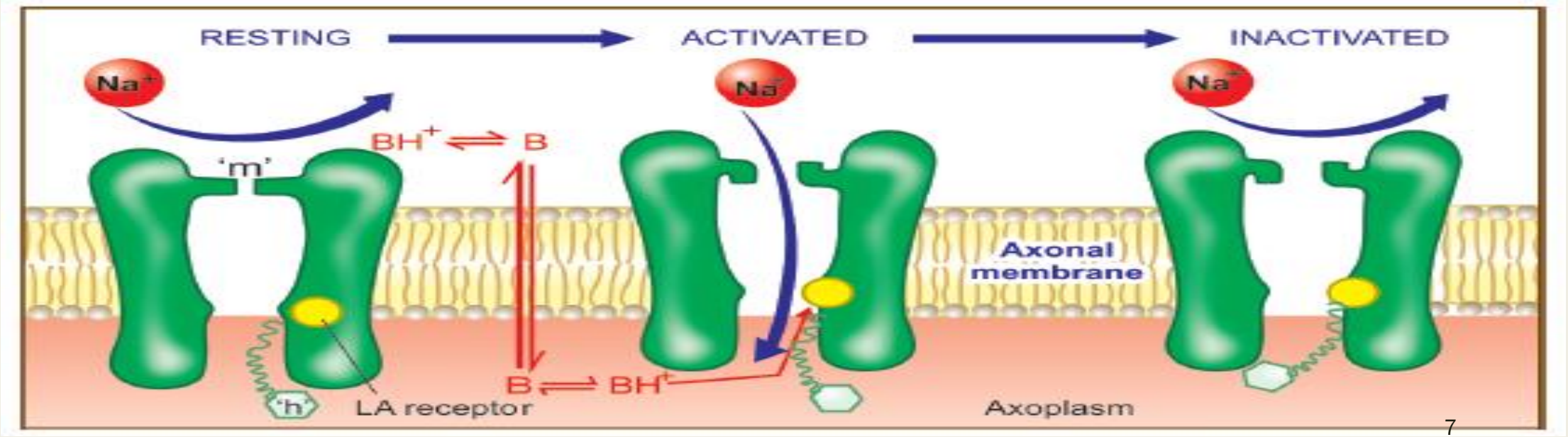
The lower the pKa, the greater the percentage of Uncharged weak base at given pH



# LOCAL ANAESTHETICS: MOA

- Site of action: Voltage gated Na channels
- Higher affinity for inactivated phase
- Voltage & time dependent
  - Less affinity for resting state
  - More effect on high frequency firing
  - Use dependent  block
- Resting potential not significantly altered

- Extracellular Calcium antagonizes
- Extracellular Potassium favours the effects
- Inflamed sites oppose the actions



# LOCAL ANAESTHETICS:MOA

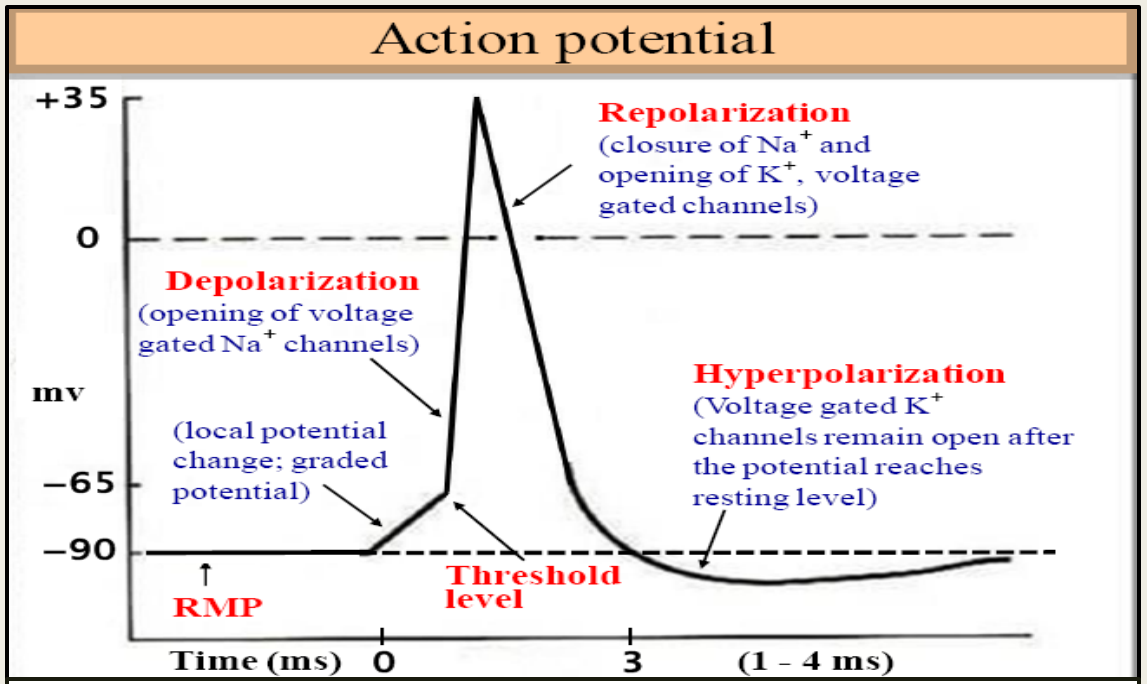
Threshold for excitation increases

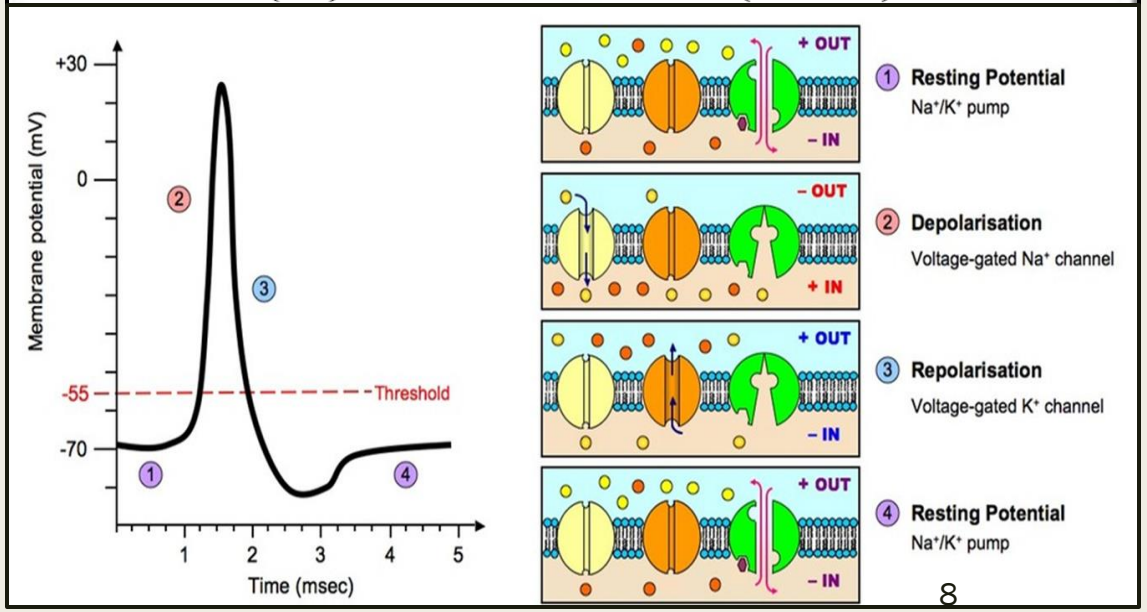
Impulse conduction slows

Rate of rise AP decreases
Action potential amplitude decreases

Ability to generate AP is abolished

Propagation blocked if Na current blocked over a critical length



# LOCAL ANAESTHETICS: PHARMACOKINETICS

- **ABSORPTION:**
  - Dosage, site of injection, drug tissue binding, local tissue blood flow, **USE OF VASOCONSTRICTOR**, physiochemical properties of drug
- **DISTRIBUTION:**
  - Localized
  - Systemic( Alpha & beta)
- **METABOLISM & EXCRETION**
  - **AMIDE TYPE:**
    - In liver
    - By cytochrome P450 isozymes
    - Effects of chronic diseases(Hepatic failure..congestive cardiac failure)
    - Drug-drug interaction( lidocaine elimination with volatile anaesthetics)
  - **ESTER TYPE:**
    - In plasma by circulating Butyrylcholinesterase
    - Short half lives( Prolonged with atypical plasma cholinesterase)

**VASOCONSTRICTOR: EPINEPHRINE**

- Blood supply limited - absorption restricted…Toxicity reduced
- Higher sustained local tissue concentrations: longer action
- Provides more bloodless field
- Delayed healing & tissue necrosis
- Spinal- direct analgesic effect $\alpha_2$ –clonidine used as adjuvant

# LOCAL ANAESTHETICS

- **OTHER SITES OF ACTION:**
  - Ion channels(Potassium & Calcium)
  - Enzymes(Adenylate cyclase)
  - Receptors(NMDA, G-Protein coupled, 5-$HT_3$)
- **FACTORS AFFECTING ACTIONS:**
  - **Structure activity characteristics:**
    - Lipophilicity
    - Lipid solubility
    - Particle size
  - **Neuronal factors affecting block:**
    - Differential block
    - Intrinsic susceptibility of nerve fibres
    - Anatomic arrangement

- **SUSCEPIBILITY OF NERVE FIBRES TO LOCAL ANESTHETICS**
- Firing frequency
- Size
- State of myelination
- Fibre diameter
- Fibre position
- Pain sensation>temperature>touch>deep pressure> motor

# LOCAL ANAESTHETICS

- **COCAINE**
  - Sympathomimetic action
  - Potent vasoconstrictor
  - Cardiac stimulation
  - Marked pyrexia with overdose
- **BENZOCAINE**
  - Profound lipophilicity
  - Topical local anaesthetic
  - Relief of pain & irritation
  - Anaesthesia of mucous membranes
  - PABA derivatives – antagonize effect of sulphonamides locally
- **LIDOCAINE(XYLOCAINE)**
  - Most widely used
  - Effective by all routes but oral BA low
  - High 1st pass metabolism
  - Fast onset, more intense & lasting effect
  - Alternative for ester allergic pts
  - Toxicity equal to procaine but more sedative than others

# LOCAL ANAESTHETICS

- **BUPIVACAINE**
  - Not effective topically
  - Slower onset, longer acting
  - Popular for anaesthesia during labour
  - More cardio toxic
  - Bupivacaine toxicity
- **EMLA**
  - **E**utectic **M**ixture of **L**ocal **A**naesthetics
  - 2.5% Lidocaine & 2.5% Prilocaine
  - Permits penetration in keratinized layers of skin
  - Used in paeds

# CLINICAL APPLICATIONS OF LOCAL ANESTHETICS

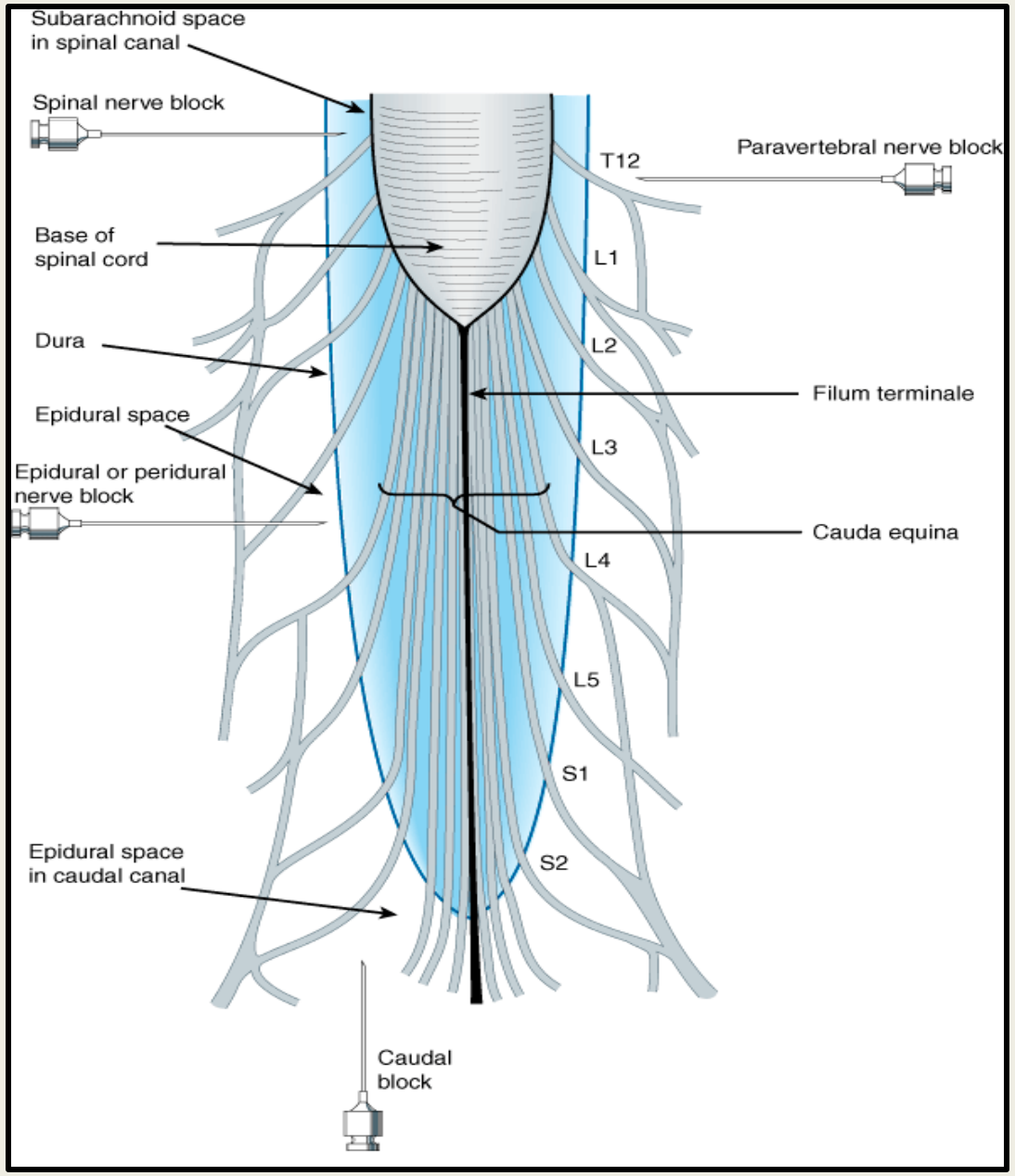
**LOSS OF SENSATIONS:**

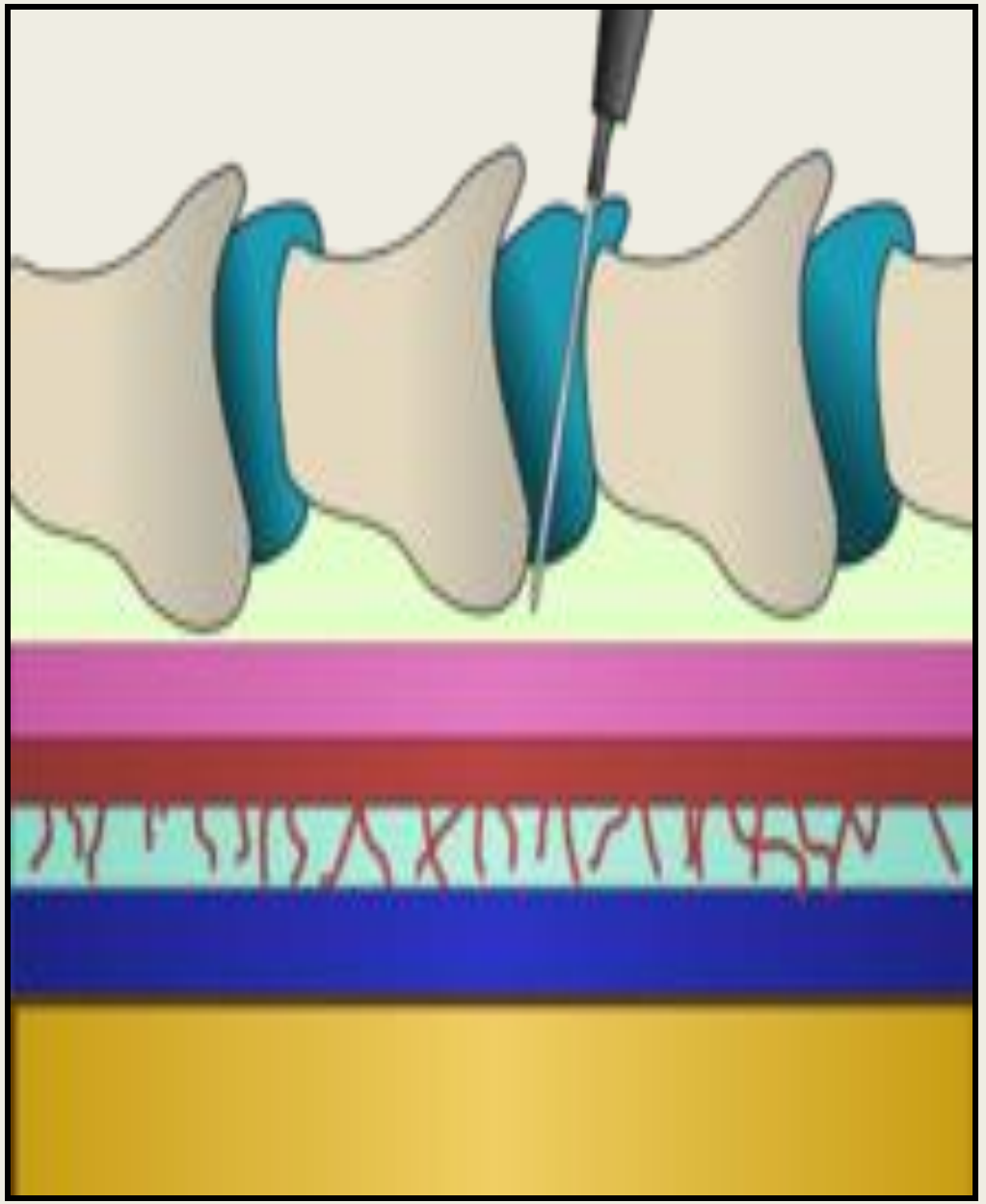
Temperature….pain…light touch….motor block

**INTENTIONAL USE OF SYSTEMIC LOCAL ANAESTHETICS:**

**(Low , moderate & high concentration)**

- **SURFACE ANESTHESIA**
  - Ear, eye, nose, throat, abraded skin
  - Only superficial layer
  - Soluble LA – rapid systemic absorption
  - Eutectic lidocaine/prilocaine – intact skin
- **INFILTRATION ANESTHESIA**
  - Dilute solution infiltrated under skin
  - Immediate onset & DoA is short
  - Minor operations: incisions, excisions
- **FIELD BLOCK or NERVE BLOCK**
  - Injected around nerve trunk
  - Area distal to injection is anesthetized & paralyzed
  - Lidocaine
  - Bupivacaine for longer
- **BIER BLOCK**
  - Intravenous regional block
  - Short surgical procedures
  - Upper or lower extremities


Subarachnoid space
in spinal canal
Spinal nerve block
Paravertebral nerve block
T12
Base of
spinal cord
L1
Dura
L2
Filum terminale
Epidural space
L3
Epidural or peridural
nerve block
Cauda equina
L4
L5
S1
Epidural space
in caudal canal
S2
Caudal
block



# CLINICAL APPLICATIONS OF LOCAL ANESTHETICS

- **SPINAL ANESTHESIA**
  - Subarachnoid space L2-3 or L3-4 – cauda equina
  - Abdominal or pelvic surgery
  - Effective analgesia & muscle relaxation
  - Complications: respiratory paralysis, hypotension (sympathetic reflexes inhibited), headache, cauda equina syndrome, infection, neurotoxicity
- **EPIDURAL**
  - Injection into epidural space at L2-3
  - Used in obstetrics, lower abdomen & pelvic surgery
  - Unwanted effects similar to spinal but less because longitudinal spread is reduced
  - Lidocaine, bupivacaine, ropivacaine

# LOCAL ANAESTHETICS: TOXICITY

## A) SYSTEMIC TOXICITY

- Absorption from site of administration

- **CNS TOXICTY**
  - Sedation, restlessness, visual & auditory disturbances
  - Circumoral & tongue numbness, metallic taste
  - Nystagmus, muscle twitching, tonic-clonic convulsions
  - Depression of cortical inhibitory pathways-unopposed activity of excitatory neuronal pathways.....Seizure activity.....Generalized CNS depression
  - Death due to respiratory failure
  - Prophylaxis-Diazepam

# LOCAL ANAESTHETICS: TOXICITY

- **CARDIOTOXICITY**
  - Direct effects on cardiac & smooth muscle membranes
    - Myocardial depression
    - Arteriolar dilation-hypotension
  - Indirect effects on ANS
  - Slow atrioventricular rhythm & broad QRS complexes
  - Bupivacaine is more cardio toxic than others.....Ventricular tachycardia & Fibrillation---ropivacaine
  - **Reversal of Bupivacaine toxicity- iv infusion of lipid**
  - Cocaine blocks norepinephrine reuptake- vasoconstriction & hypertension, cardiac arrhythmias

# LOCAL ANAESTHETICS: TOXICITY

- HEMATOLOGICAL
  - Prilocaine – metabolite O-toluidine
  - An oxidizing agent converts Hb to meth Hb
- ALLERGIC REACTONS
  - Esters converted to p -aminobenzoic acid (PABA) derivatives

B) DIRECT NEUROTOXICITY

- Local effects when high concentrations are administered in close proximity to the spinal cord and other major nerve trunks
  - NEURAL INJURY
    - More with Chloroprocaine and lidocaine
    - Transient radicular irritation or neuropathic pain
    - Interference with axonal transport and disruption of calcium homeostasis
    - Cauda equina syndrome
  - TRANSIENT NEUROLOGIC SYNDROME

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- A vasoconstrictor added to a solution of lidocaine for a peripheral block will
  - Decrease the risk of seizures
  - Increase the duration of anaesthetic action of local anaesthetic agent
  - Both A & B
  - Neither A & B

Both A & B

- Which statement about the speed of onset of nerve blockade with local anaesthetics is correct?
  - Faster in hypercalcemia
  - Faster in myelinated fibres
  - Faster in tissues that are infected
  - Slower in hyperkalaemia
  - Slower in the periphery of nerve bundle than in the centre of the bundle

Faster in myelinated fibres

- If pKa of Bupivacaine is 8.3.In infected tissue which can be acidic , for example at pH 6.3, the percentage of the drug in non ionized form will be.
  - 1%
  - 10%
  - 50%
  - 90%
  - 99%

1%

# THANK YOU