

Local Anesthetic agents

211 MDS

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Definitions

- Anaesthesia is the loss of consciousness and all form of sensation.
- Local Anaesthesia is the local loss of pain, temperature, touch, pressure and all other sensation.
- In dentistry, Only loss of pain sensation is desirable (Local Analgesia)
- Local anesthetic agents
Are drugs that block nerve conduction when applied locally to nerve tissues in appropriate concentrations, acts on any part of the nervous system, peripheral or central and any type of nerve fibres, sensory or motor.

Methods of producing local anesthesia

- *Reducing temperature.*
Is used only to produce surface anaesthesia e.g. ethyl chloride spray.
- *Physical damage to nerve trunk e.g. nerve sectioning.*
Unsafe for therapeutic uses, only in some situations such as Trigeminal Neuralgia.
- *Chemical damage to nerve trunk e.g. neurolytic agents.*
Silver nitrate, Phenol - Unsafe for therapeutic use.
- *Anoxia or hypoxia* resulting in lack of oxygen to nerve.
Unsafe as well.
- *Stimulation of large nerve fibres*, blocking the perception of smaller diameter fibres.
includes Acupuncture and TENS (Transcutaneous Electronic Nerve Stimulation)
- *Drugs* that block transmission at sensory nerve endings or along nerve fibres.
Their action is fully reversible and without permanent damage to the tissues.

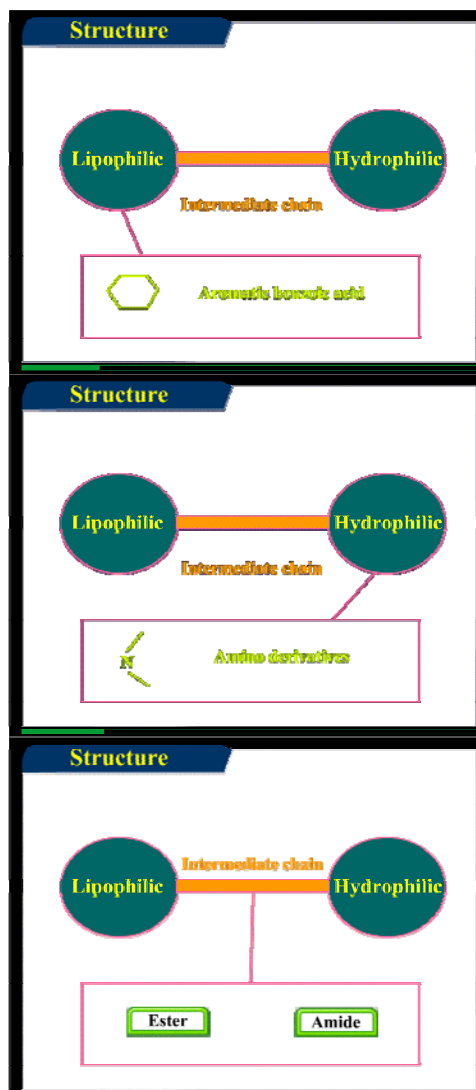
Properties of ideal Local Anesthetic agent

- Possess a specific and reversible action.
- Non-irritant with
- No permanent damage to tissues.

- No Systemic toxicity (High therapeutic ratio).
- Rapid onset
- Long duration
- Active Topically or by injection
- Non addictive
- Chemically stable
- Sterilizable without loss of properties

Chemical structure

- Chemistry:
 - **They are weak bases, insoluble in water**
 - Converted into soluble salts by adding HCl for clinical use.
 - **They are composed of three parts:**
 - *Aromatic* (lipophilic) residue with acidic group
 - *Intermediate* aliphatic chain, which is either ester or amide link
 - Terminal *amino* (hydrophilic) group



Classification of Local Anesthetics

Classified according to their chemical structures and the determining factor is the intermediate chain, into two groups:

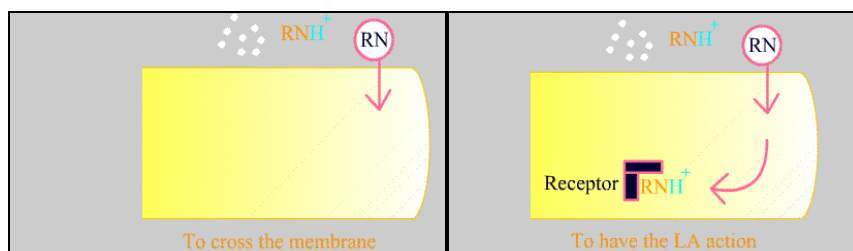
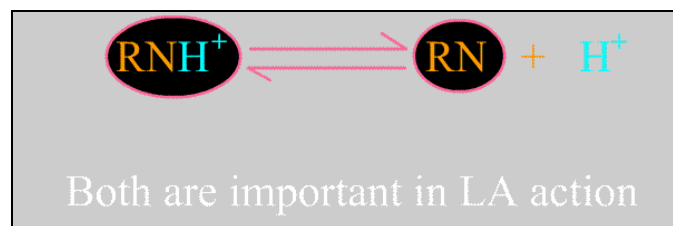
1-Ester

2-Amide

- They differ in two important respect:
 - Their ability to induce hypersensitivity reaction.
 - Their pharmacokinetics - fate and metabolism.

Physicochemical properties

- These properties are very important for local anesthetic activity.
- **Ionization:**
 - Local anesthetics are weak bases and exist partly in an unionized and partly in an ionized form.
 - The proportion of unionized and ionized depends on:
 - the pKa or dissociation constant
 - The pH of the surrounding medium.
 - Both ionizing and unionizing are important in producing local anesthesia.
 - Unionized form to cross the membrane
 - Ionized form to do the action



- **Dissociation constant (pKa):**
 - pKa is the pH at which the ionized and unionized form of an agent are present in equal amounts and it measures the affinity of molecules to hydrogen ions.
 - The lower the pKa , the more the unionized form, the greater the lipid solubility, the greater the crossing of the membrane (Rapid Onset).
 - The higher the pKa , the more the ionized form and the slower the lipid solubility, the lower the crossing (Slow Onset)
 - Unionized form is able to cross the bi-lipid nerve membrane.
 - The ionized form then blocks conduction.
 - Some of the unionized inside the cell will become ionized depending upon the pKa and the intracellular pH (lower than extracellular)

 - In general the amide type have lower pKa, and greater proportion of the drug is present in the lipid-soluble (unionized) form at the physiological pH

- **Partition coefficient:**
 - This measures the relative solubility of an agent in fat and water.
 - High numerical value means:
 - High lipid-soluble
 - less water-soluble.
 - More fat solubility means rapid crossing of the lipid barrier of the nerve sheath and rapid onset.
 - *The greater partition coefficient, The faster the onset*

- **Protein binding:**
 - Local anesthetic agents bind with glycoprotein, Albumin and red blood cells:
 - The binding is simple, reversible
 - Lignocaine is 64% bound, Bupivacaine is 96%
 - *The duration of action is related to the degree of binding.*
 - According to the protein binding Lignocaine lasts for 15 – 45 minutes while Bupivacaine for 6 hours

- **Vasodilation ability:**
 - Most Local anesthetics possess a vasodilation action on blood vessels except Cocaine.
 - This can influence the duration of action of the local anesthetic agent.
 - Prilocaine is 50% bound to proteins but has almost the same duration of Lignocaine (which binds to protein by 64%). This is because Prilocaine has no strong vasodilation effect.

- **Summary**
 - Rapid Onset:
 - Low pKa value– more unionized – Amides
 - Higher Partition coefficient – more lipid soluble
 - Long duration of action:

- High protein binding.
- Low vasodilating property.

Pharmacodynamics of Local Anesthetics

- Reversible block of conduction in nerve.
- Direct relaxation of smooth muscle & inhibition of neuro-muscular transmission in skeletal muscle producing vasodilation.
 - Intra-arterial procaine is used to reverse arteriospasm during I.V. Sedation
- Class I antidysrhythmic-like action on the heart.
- Stimulation and/or depression of the CNS.

■ **Absorption:**

- Many factors influence entry of local anesthetic into the circulation:
 - Vasodilating ability of the drug.
 - Volume and concentration.
 - Vascularity of the tissues.
 - The route of administration.
 - The presence of vasoconstrictor.

Local anesthetic agents

Ester type Local Anesthetic agents

■ **Cocaine:**

- The first and most potent local anesthetic agent, rarely used because of the problems of misuse.
- It is unique in its ability to produce intense vasoconstriction. Half life 30 minutes.
- Dosage:
 - Used as topical 4 – 10% solution
 - Maximum dose is 1.5 mg/kg – 100mg max.

■ **Procaine:**

- The only indication for its use in dentistry is in patients with proven allergy to the amide group.
- Used intra-arterially, as part of the recognized regimen, to treat the arteriospasm which might occur during intravenous sedation.
- It has an excellent vasodilatory properties.
- Onset & duration of Action:
 - Has a very short duration (5 minutes) and a long onset time of 10 minutes
- Dosages:

- The maximum dose is 6 mg/kg, 400 mg max.
 - Used as 2% with 1:80,000 epinephrine to increase efficacy.
- Metabolism:
 - Rapidly metabolised by plasma esterase.

- **Benzocaine:**
 - Used mainly as topical, due to its poor water solubility, and because of its low toxicity, it is used in concentration up to 20%.

 - Hydrolyzed rapidly by plasma esterase to paraortho-aminobenzoic (PABA) acid accounting for its low toxicity.

- **Metabolism of Ester drugs:**
 - Metabolized in plasma by pseudocholinesterase enzyme, and some in the liver.
 - People, who lack the enzyme, are at risk of an overdose by the ester type local anesthetic
 - Para-aminobenzoic acid (PABA) is the major metabolite of ester with no anaesthetic effect (It is the agent responsible for ester allergies).

Amide type Local Anesthetic agents

- **Lignocaine (Lidocaine, Xylocaine):**
 - Synthesized in 1943 and used in dentistry since 1948
 - It highly lipophilic (partition coefficient 3) , rapidly absorbed.
 - Metabolized in the liver and its metabolites are less toxic
 - Has half-life ($t_{0.5}$) of 90 minutes
 - Dosage:
 - 4.4 mg/kg – 300 mg max
 - Used as 2% plain or with 1:80 000 epinephrine
 - 4 and 10% spray, 2% gel and 5% ointments.
 - **Onset & duration of action:**
 - Rapid onset 2 – 3 minutes
 - Plain (no vasoconstrictor)- short duration (10 minutes)
 - With epinephrine- intermediate duration (45 – 60 minutes)

- **Prilocaine:**
 - A very potent local anaesthetic and is less toxic than Lignocaine.
 - It produces less vasodilatation than lignocaine
 - Rate of clearance is higher than other amide-types, suggesting extra-hepatic metabolism with relatively low blood concentration.
 - It's metabolite o-toluidine leads to methaemo-globinaemia (more than 600 mg in adults)

- Used either plain 4% or 3% combined with 0.03IU/mL of Felypressin as vasoconstrictor.
 - Onset & Duration:
 - Slower onset – 4 minutes.
 - It's duration of action is similar to Lignocaine.
 - Dosage;
 - 6.0 mg/kg – max. 400 mg.
 - Combined with Lignocaine as a topical anesthetic (EMLA)
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- **Mepivacaine:**
 - Possess the least vasodilating effect.
 - Metabolized in the liver and has a *half life* of 120 minutes.
 - It's main indication is when local anaesthetic without vasoconstrictor is needed. 3% plain is more effective than lignocaine.
 - Onset & duration:
 - Rapid onset but slightly shorter duration than Bupivacaine.
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- **Bupivacaine:**
 - A long-acting local anesthetic agent, with a *t_{0.5}* of 160 minutes due grater binding capacity to plasma protein and tissue proteins
 - Metabolized in the liver.
 - Used mainly in Oral surgical procedures for its long-lasting pain control.
 - Longer onset and longer duration (Regional 6 – 8 hors)
 - Dosage:
 - 1.3 mg/kg – Max 90 mg
 - 0.25 – 0.75% with or without adrenaline 1:200 000
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- **Etidocaine:**
 - A long-acting agent similar to Bupivacaine but with faster onset.
 - Metabolized in the liver.
 - Dosage:
 - 8 mg/kg – Max 400 mg
 - 1.5% with 1:200 000 epinephrine.
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- **Fate and metabolism of Amide Local Anesthetic agents:**
 - metabolized in the liver, except Prilocaine which undergo some biotransformation in the kidney and lungs.
 - Some of the metabolites possess local anaesthetic and sedative properties.
 - Normal local anaesthetic dose in patient with impaired liver function will result in relative overdose so reduce the dose according to the age, weight and medical status of the patient.
 - Old age patient shows reduction in liver function so you have to be careful with dose

Contents of Local Anesthetic cartridge

- Local anesthetic agent
 - e.g. xylocaine

- Vasoconstriction
 - e.g. adrenaline
 - To decrease the toxicity, increase the duration and decrease bleeding

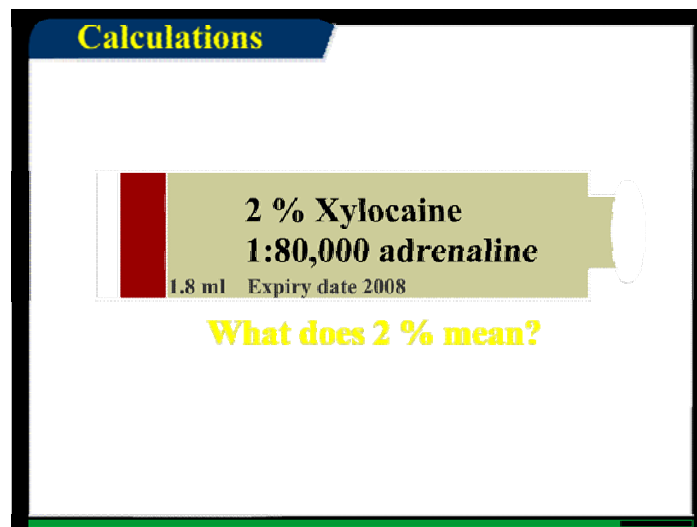
- Antioxidant
 - Sodium metabisulfite
 - To prevent oxidation of vasoconstrictor

- Isotonic buffer
 - Sodium chloride
 - To make the solution isotonic with tissues

- Distilled water
 - To provide the volume of solution

- Preservative
 - Methylparaben
 - Bacteriostatic/fungistatic agent
 - It is the cause of allergy

How to calculate the amount of local anesthetic agent in the cartridge



2% Xylocaine means

2 grams of Xylocaine in 100 ml of solution

In the Local anesthetic cartridge we have 1.8 ml

So how many grams of xylocaine in 1.8 ml

$$\begin{array}{l} 2\text{g}----- 100 \text{ ml} \\ ??----- 1.8 \text{ ml} \end{array}$$

$$= 2 \times 1.8 / 100 = 0.036 \text{ g}$$

$$1 \text{ gram} = 1000 \text{ mg}$$

$$\text{So } 0.036\text{g} = (0.036 \times 1000) = 36\text{mg}$$

So each 1.8 ml contains 36 mg of xylocaine

Adult maximum dose of xylocaine is 300 mg

$$300\text{mg}/36\text{mg} = 8.3$$

So the maximum number of cartridges that can be given to the patient is 8