牙科麻醉學
**Dental anesthesiology**

# Pharmacology of local anesthetic and Clinical Notes in Local Anesthesia

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## Purpose

1.Physical and psychological evaluation prevention of emergencies

2.Management of medically or Mertally compromised out patient 3.General anesthesia 4.Dental local or nerve block anesthesia

## Reference

1.Handbook of local anesthesia Stanley F.Mclamed 1997 4th ed. Mosby

2.Handbook of local anesthesia Stanley F.Mclamed 1995 3th ed. Mosby 3.Sedition

## Summary

- Introduction of dental anesthesiology
- Pharmacology of local anesthetic and Clinical Notes in Local Anesthesia
- Peri-op management of anesthesia
- General Anesthesia and Sedation
- Anesthesia and Co-existing Diseases
- ACLS and Airway Management
- ACLS
- Local Anesthesia In Dentistry
- Sedation in dentistry

## Topics

- **Introduction of anesthesia**
- **Pharmacology of local anesthetic agents**
- **Various techniques commonly used for local anesthesia,**
- **Special emphasis on safety.**
- **Clinical features of toxicity,**

## Anesthesia

- **Anesthesia is the loss of sensitivity to pain brought about by various drugs ( Beta-adrenoceptor antagonists, opioid analgesics, anticonvulsants and antihistamines. Anesthetic etc.)**
- **Anesthesia is used during many medical procedures, including surgical procedures.**
- **Local anesthetics are safer than general or systemic anesthetics; therefore, they are used whenever possible**

## Introduction of Anesthesia

- **Anesthesia can be categorized by the degree to which it suppresses consciousness and protective reflexes.**
- **Larger procedures often require greater amounts of anesthesia.**
- **From least to most, levels of anesthesia include: *local, conscious sedation, regional and general.***
- **Determining the best choice for you depends on the anticipated nature and duration of the procedure, as well as your medical and psychological health.**

## Types of Anesthesia

- **Local anesthesia is used to block pain in a specific part of your body, allowing you to remain fully alert.**
- **Conscious sedation or intravenous (IV) sedation is used to relax you and make you feel sleepy .**
- **Regional anesthesia is used to block sensation in a particular region of your body, such as the lower half of your body, an eye, or an arm or leg.**
- **General anesthesia is used for more extensive procedures or for procedures that aren't amenable to regional anesthesia.**

## Choice of Type of Anesthesia

- **The type of anesthesia you receive depends on the procedure being performed and your physical and emotional status.**
- **Knowing the type of anesthesia you will receive before a medical procedure or surgery will help you know what to expect in terms of preparation, pain relief and recovery.**

## Introduction of Local anesthesia

- **An increasing number of minor surgical procedures are performed under local anaesthesia in clinical settings outside the operating room.**
- **Monitoring and resuscitation equipment , personnel skilled in resuscitation— not available.**
- **Serious adverse effects --- such as systemic toxicity, allergy, vasovagal syncope, and reaction to additives present in the local anaesthetic.**

## Local anesthesia

- The area -- small and superficial.
- For dental work, skin biopsies or wound repair.
- For a more extensive procedure is not in advisable – consider general or regional anesthesia.
- Anesthetic agents was injected at or near the site of the procedure.
- The injection numbs the area to pain and any other sensation.

## Techniques of Local Anesthesia

- Topical anesthesia,
- Infiltrative anesthesia,
- Ring blocks,
- Peripheral nerve blocks.

## Introduction of Local Anesthetics

- A local anesthetic is an agent that interrupts pain impulses in a specific region of the body without a loss of patient consciousness.
- Normally, the process is completely **reversibl**e-- the agent does not produce any residual effect on the nerve fiber.
- Local anesthetics are generally of short duration -- in different forms, including injections, sprays and ointments.

## History of Anesthetic Agent

**Although the medical world cannot cure every disease, the control of pain to ensure patient comfort should be a goal.**

## 南美洲古柯鹼(Coca)

古柯鹼來自古柯樹的葉子，可說是早期南美洲土人的零食。十九世紀時，歐洲探險家見到南美洲土人咀嚼一種灌木樹葉後，不需進食就可長期勞動，因此懷疑葉子內的某些成分可使人增加體力、不易疲勞。他們便將樹葉帶回歐洲研究，最後在沃勒（F. Wohler）的實驗室中分離得到能令人舌頭麻木的古柯鹼（cocaine）。

當時除了德國默克公司萃取這類化合物給生理學家進行實驗外，也有人把古柯葉拿來調酒。

美國早期生產的「可口可樂」亦含有古柯葉萃取物（一九〇四年後被美政府禁用）。從可口可樂的名字上就可看出端倪。它的其中兩種成分就是古柯(Coca)的葉子和可樂(Kola)的果實，將Kola 的K 改為C，然後在兩個字的中間加上一橫，Coca-Cola 便誕生了。

到了二十世紀，純化的古柯鹼受到一些知識份子的讚揚，以至於愈來愈多人被吸引，終致形成嚴重的濫用情形。古柯鹼的用量越來越大，其成癮效果對社會的影響也越來越大


- 從1886 年到1903 年，可口可樂裡一直都含有古柯鹼.
  可口可樂一直是作為一種藥酒，美國南方則把它當麻醉飲料飲用
  成分就是古柯(Coca)的葉子和可樂(Kola)的果實----- Coca-Cola


## Coca—(A natural anesthetic agent)

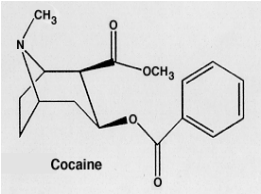
- **Coca** is a plant in the family Erythroxylaceae, native to north-western South America.
- The plant plays a significant role in traditional Andean culture.
- Its leaves are used by Andean cultures for medicinal and ceremonial purposes, and consumed for their mild stimulant effects either by chewing or as an herbal tea.
- Coca leaves are also the raw material from which the stimulant drug cocaine is extracted by a chemical process.

## History

- In 1860, cocaine, the oldest anesthetic, was extracted from the leaves of the Erythroxylon coca bush.
- In 1884, Sigmund Freud and Karl Koller were the first to use it as an anesthetic agent during ophthalmologic procedures.
- Freud who used it to wean a patient from morphine addiction.
- Freud and his colleague Karl Kollar who first noticed its **anesthetic effect**.
- **Hall introduced it to dentistry**.
- In 1884, Dr. William Stewart Halsted was the first to describe the injection of cocaine into a sensory nerve trunk **to create surgical anesthesia.**

## Cocaine

It is applied to certain areas of the body to cause loss of feeling. (eg, the nose, mouth, or throat)




## Development of Anesthetic Agent

Procaine---a synthetic alternative to cocaine was not developed until 1904.

Para-aminobenzoic acid (PABA), is metabolite of procaine, is a known allergen .

Tetracaine, another ester-type anesthetic, was introduced in 1930.

Tetracaine is more potent than procaine, it causes similar allergic reactions.

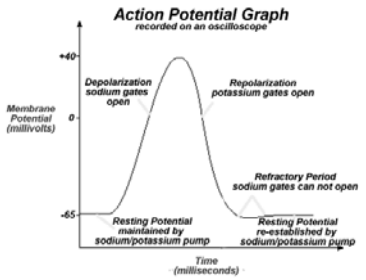
## Development of Anesthetic Agent

- In 1943, an alternative class of anesthetics was discovered when Lofgren developed lidocaine.
- This agent is an amide derivative of diethylaminoacetic acid, not PABA; therefore, it has the benefit of a low allergic potential.
- Multiple amide-type anesthetics have been introduced into clinical use.
- Slight chemical alterations to the compounds have imparted beneficial characteristics, including increased duration and potency, to each.
- These compounds offer the surgeon more choices, and anesthetics can be appropriately matched to different procedures.

## Mechanism of Action

## Physiology of nerve conduction

- Nerves transmit sensation as a result of the propagation of electrical impulses; this propagation is accomplished by alternating the ion gradient across the nerve cell wall, or axolemma.



## Mechanism of action

- **Local anesthetics inhibit depolarization of the nerve membrane by interfering with both Na+ and K+ currents.**
- **The action potential is not propagated because the threshold level is never attained.**

## Mechanism of action

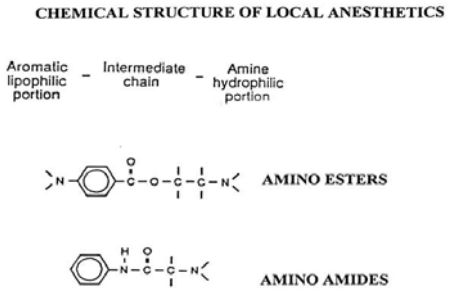
- 1) slow rate of depolarization
- 2) reduce height of action potential
- 3) reduce rate of rise of action potential
- 4) slow axonal conduction
- 5) ultimately prevent propagation of action potential
- 6) do not alter resting membrane potential
- 7) increase threshold potential

## Types of Nerve fibers

- Type A fibers are the largest and are responsible for conducting pressure and motor sensations.
- Type B fibers are myelinated and moderate in size.
- Type C fibers, which transmit pain and temperature sensations, are small and unmyelinated.
- Anesthetics block type C fibers more easily than they do type A fibers. Therefore, patients who have blocked pain sensation still feel pressure and have mobility because of the unblocked type A fibers.

## Chemistry

All local anesthetics are weak bases, classified as tertiary amines.




## local anesthetics

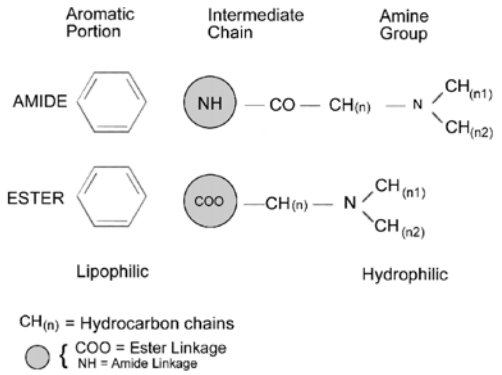
All have a similar chemical structure, consists of 3 components:

- an aromatic portion,
- an intermediate chain,
- an amine group

The aromatic portion, usually composed of a benzene ring, is lipophilic, whereas the amine portion of the anesthetic is responsible for its hydrophilic properties.

## Local anesthetics are classified into 2 groups:

- The classification is based on the chemical structure of the intermediate chain.
- This structural difference affects the pathway by which local anesthetics are metabolized and the allergic potential.



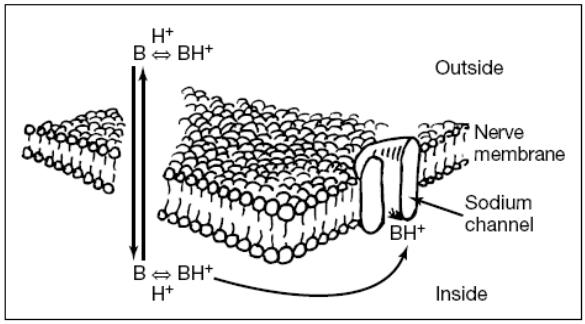




**Fig. Local anaesthetics exist in non-ionised (B) and ionised ($BH^+$) forms in physiological solution**

- The degree of lipid solubility of each anesthetic is an important property because its lipid solubility enables its diffusion through the highly lipophilic nerve membrane.
- The extent of an anesthetic's lipophilicity is directly related to its potency.

## Esters-type local anesthetics

- These include cocaine, procaine, tetracaine, and chloroprocaine.
- They are hydrolyzed in plasma by pseudo-cholinesterase. One of the by-products of metabolism is seen with these agents
- ***Paraaminobenzoic acid*** **(PABA)**, the common cause of allergic reactions
- In patients with a known allergy to an ester anesthetic, the use of all other ester-type anesthetic agents should be avoided

## Amide-type local anesthetics (Two i)

- These include *lidocaine, mepivicaine, prilocaine, bupivacaine, and etidocaine.*
- They are metabolized *in the* ***liver*** *to inactive agents.* The specific microsomal enzyme responsible for the elimination of lidocaine is cytochrome P-450 3A4.
- True allergic reactions are rare (especially with lidocaine)

## Factors Affecting Anesthetic Action

- Lipid solubility -- more lipophilic agents are more potent
- Diffusibility -- increased diffusibility = decreased time of onset
- Affinity for protein binding--- increased binding increases duration of action
- Ionization at physiologic pH-- ionized and nonionized forms --vary with the pH of the environment.
- Vasodilating properties.-- greater vasodilator activity = decreased potency and decreased duration of action

## Factors affecting anesthetic action (A)

- **Dosage of local anesthetic solutions**
- **Site of injection—**
- **Addition of vasoconstrictors**
- **Use of additives with local anaesthetics**
- **Lipid solubility -- more lipophilic agents are more potent**
- **Diffusibility -- increased diffusibility = decreased time of onset**
- **Affinity for protein binding--- increased binding increases duration of action**

## Factors affecting anesthetic action (B)

- **Ionization at physiologic pH-- ionized and nonionized forms --vary with the pH of the environment.**
- **Vasodilating properties.-- greater vasodilator activity --decreased potency and decreased duration of action**

Table 1. **Local Anesthetics Used in Laceration Repair.***

| Agent | Duration of Action | Maximum Dose | Maximum Volume for a 70-kg Patient |
|---|---|---|---|
| | *min* | *mg/kg of body weight* | *ml* |
| 1% Lidocaine | 30 | 4.5 | 31.5 |
| 1% Lidocaine with epinephrine | 60–240 | 7 | 49 |
| 0.25% Bupivacaine | 240–480 | 3 | 84 |

* A 1% solution is equal to 1 g of agent per 100 ml of diluent. Therefore, each milliliter of a 1% solution of lidocaine contains 10 mg of the agent. Data are from Trott.[3]

- Adding sodium bicarbonate (1 mmol/10 mL LA solution) to lignocaine decreases the onset time after epidural injection by increasing the amount of non-ionized drug (because of the more alkaline medium).
- ***Mixtures of local anaesthetics*** thus limiting its toxicity, and to combine the rapid onset of one drug with the long duration of the other,

- Lidocaine buffered with bicarbonate to decrease discomfort associated with the initial injection as well as to enhance tissue diffusion and speed the onset of the anesthetic.
- Typically, 1mEq of sodium bicarbonate is added to each 10mL of lidocaine or mepivacaine; only 0.1mEq of sodium bicarbonate may be added to each 10mL of bupivacaine to avoid precipitation

**Table 15.5. Data related to local anaesthetic toxicity**

| Drug | Relative potency[a] | Approximate protein binding[b] (%) | Onset time | Duration of action | Maximum dose (70-kg man) (mg) |
|---|---|---|---|---|---|
| Prilocaine | 2 | 55 | Fast | Medium | 600 |
| Lignocaine | 2 | 65 | Fast | Medium | 200[c] |
| Ropivacaine | 6 | 95 | Medium | Long | 200[d] |
| Bupivacaine | 8 | 95 | Medium | Long | 150[e] |

[a]Potency is determined by lipid solubility.
[b]Drugs with high protein binding attach strongly to active sites and have prolonged duration of action.
[c]This can be increased to 400 mg with addition of epinephrine for field blocks.
[d]Maximum dose inferred from product data sheet.
[e]This can be increased to 200 mg with addition of epinephrine for field blocks.

## Toxicity and adverse effects of local anesthetics

## Allergic reactions

- Allergic reactions to local anesthetics are extremely rare, especially with amide local anesthetics, and account for less than 1% of the reactions caused by local anesthetics.
- Reactions can be type 1 (ie, anaphylactic) or type 4 (ie, delayed-type hypersensitivity) reactions.
- These reactions are not dose related, but, they are idiosyncratic.

## Allergic reactions

- Type 1 reactions are usually caused by ester-type anesthetics.
- The ester group of local anesthetics have a much greater allergenic potential than that of the amide group.
- Pseudocholinesterases, which produce the highly allergenic metabolic product PABA, break down ester-type anesthetics.
- Cross-reactivity exists among ester anesthetics; therefore, the use of all anesthetics in this structural group should be avoided in a patient with an established sensitivity to one ester-type anesthetic.

## Allergic reactions

- Clinical signs of type I reactions include pruritus, urticaria, facial swelling, wheezing, dyspnea, cyanosis, laryngeal edema, nausea, vomiting, and abdominal cramping.
- Epinephrine with a concentration of 1:1000 should be subcutaneously administered at a dose of 0.3-0.5 mL.
- This dose can be repeated every 20-30 minutes to a maximum of 3 doses.
- If anaphylaxis ensues, a 5-mL dose of epinephrine 1:10,000 should be administered intravenously.

- Type IV (ie, delayed-type hypersensitivity) reactions account for 80% of allergic reactions to local anesthetics.
- They are more common with the use of topical anesthetics and may occur with anesthetics of the amide and ester subtypes.
- Clinical manifestations are similar to those of allergic contact dermatitis and include erythema, plaques, and pruritus.
- Patients with a history of type IV reactions are not at an increased risk of type I reactions due to amide-type anesthetics.
- Contact dermatitis caused by topical anesthetics should be treated with topical steroid preparations.

## Side effects

- **Adverse effects often relate to technique of local anesthesia rather than the properties of the medication.**
- **Risk of adverse effects increases with increased systemic absorption (excess dose, rapid absorption, delayed elimination, accidental intravenous administration) --**

***Overdose !!!!!***

- Local anesthetics, **with the exception of cocaine**, are vasodilators.
- This occurs via direct relaxation of peripheral arteriolar smooth muscle fibers.
- Greater vasodilator activity of a local anesthetic leads to faster absorption and, thus, shorter duration of action.
- **To counteract this vasodilatation, *epinephrine*** often is included in local anesthetic solutions.

## Vasoconstrictors

**Why ?**

**We used vasoconstrictor.**

## Addition of epinephrine to the local anesthetic solution

- May improve safety and allow administration of lower doses of local anesthetic.
- Induces vasoconstriction, delaying absorption of the local anesthetic for **longer duration of action** at the site of injection.
- Improves hemostasis of the operative field, which may decrease prolonged local anesthetic effect.

## Epinephrine has its own toxicities

- **Cardiac arrhythmias** may be produced in patients with heart disease or with the concomitant use of halothane anesthesia.
- **Hypertension** may develop in patients with a preexisting history of hypertension, hyperthyroidism.

severe coronary artery disease and dysrhythmias.

DM

## Practical Point

- Adrenaline 1:1000 contains 1 gram of adrenaline per 1000mls solution i.e. 1mg/ml.
- To prepare a 1 in 200,000 solution the 1:1000 must be diluted 200 times.
- This is achieved by taking 0.1c.c. (= 0.1mg) and adding 19.9 mls of local anaesthetic solution.

| Anesthetic | Duration Without Epinephrine, min | Duration With Epinephrine, min | Maximum Dose Without Epinephrine, mg/kg | Maximum Dose With Epinephrine, mg/kg |
|---|---|---|---|---|
| **Esters** | | | | |
| Cocaine | 45 | - | 2.8 | - |
| Procaine | 15-30 | 30-90 | 7.1 | 8.5 |
| Chloroprocaine | 30-60 | - | 11.4 | 14.2 |
| Tetracaine | 120-240 | 240-480 | 1.4 | - |
| **Amides** | | | | |
| Lidocaine | 30-120 | 60-400 | 4.5 | 7 |
| Mepivacaine | 30-120 | 30-120 | 4.5 | 7 |
| Bupivacaine | 120-240 | 240-480 | 2.5 | 3.2 |
| Etidocaine | 200 | 240-360 | 4.2 | 5.7 |
| Prilocaine | 30-120 | 60-400 | 5.7 | 8.5 |

**Signs and symptoms of local anesthetic toxicity (with increasing plasma concentration)**

- CNS--
- CV --

## Cardiovascular toxicity

- slowing of the conduction in the myocardium
- myocardial depression
- peripheral vasodilatation
- usually seen after 2 to 4 times the convulsion dose has been injected

**Signs and symptoms of local anesthetic toxicity (with increasing plasma concentration)**

- Numbness of tongue
- Lightheadedness
- Visual and auditory disturbances
- Muscular twitching
- Unconsciousness
- Convulsions
- Coma
- Respiratory arrest
- Cardiovascular depression

Systemic Toxicity of Local Anesthetics

This can be minimized by

- 1) aspiration prior to injection,
- 2) use of epinephrine-containing solutions for the test dose, and
- 3) use of small incremental doses, increasing the total injection time

## Factors affecting systemic toxicity

- Potency of the local anesthetic
- Total dose administered
- Addition of exogenous vasoconstrictor
- Vascularity of the tissues
- Rate of systemic uptake
- Patient's acid-base status

## Treatment of local anesthetic toxicity

Apparent allergy

- Steroids
- Histamine (H1) blockers
- With severe reactions
  - Intravenous fluid
  - Epinephrine

CNS toxicity

- Don't treat minor reactions
- Seizures: maintain airway, provide $O_2$
  - Terminate seizure with thiopental, midazolam, or propofol
  - Intubate patients with full stomachs

- Bupivacaine toxicity includes cardiac arrest and ventricular arrhythmia refractory to treatment.
- Care should be taken to avoid large volumes
- Epinephrine should not be injected into the digits, penis, nose, or ears
- Do not exceed maximum dosing recommendations for individual anesthetic—
- **Preparation---Pay Attention!!!!**

## Treatment of local anesthetic toxicity

Apparent allergy
- Steroids
- Histamine (H1) blockers
- With severe reactions
  - Intravenous fluid
  - Epinephrine

CNS toxicity
- Don't treat minor reactions
- Seizures: maintain airway, provide $O_2$
  - Terminate seizure with thiopental, midazolam, or propofol
  - Intubate patients with full stomachs

**Treatment of systemic local anaesthetic toxicity**

*Airway*
Establish clear airway; suction, if required

*Breathing*
Oxygen with face mask
Encourage adequate ventilation
Artificial ventilation, if required

*Circulation*
Elevate legs
Increase IV* fluids if ↓ blood pressure
CVS† support drug if ↓ blood pressure persists or ↓ heart rate
Cardioversion for ventricular arrhythmias

*Drugs*
Central nervous system depressant
- Diazepam 5-10 mg IV, midazolam 2-5 mg
- Thiopental 50 mg IV, incremental doses until seizures cease CVS support
- Atropine 0.3-0.6 mg IV, if ↓ heart rate
- Ephedrine 15-30 mg IV, to restore adequate blood pressure
- Adrenaline for profound cardiovascular collapse

* IV Intravenous
† CVS cardiovascular system

## Technique of Administration

Pain on injection can be reduced using:
- A solution warmed to body temperature
- A small needle (27 or 30 gauge)
- A slow injection
- A subcutaneous rather than intradermal injection technique
- A topical anesthetic 'premed' such as EMLA cream
- Ice or ethyl chloride to cool the area prior to injection

## Administration of local Anesthetics

**Consider :**
- the individual characteristics of the patient,
- dose of local anesthetic to be administered,
- presence or absence of epinephrine,
- speed of administration,
- local tissue vascularity,
- technique of administration.

- ***smallest dose possible administered***