# Chapter 26 Local Anaesthetics

Local anaesthetics (LAs) are drugs which upon topical application or local injection cause reversible loss of sensory perception, especially of pain, in a restricted area of the body. They block generation and conduction of nerve impulse at any part of the neurone with which they come in contact, without causing any structural damage. Thus, not only sensory but also motor impulses are interrupted when a LA is applied to a mixed nerve, resulting in muscular paralysis and loss of autonomic control as well.

Important differences between general and local anaesthesia are tabulated in Table 26.1.

## CLASSIFICATION

### *Injectable anaesthetic*

*Low potency, short duration*
- Procaine
- Chloroprocaine

*Intermediate potency and duration*
- Lidocaine (Lignocaine)
- Prilocaine

*High potency, long duration*
- Tetracaine (Amethocaine)
- Bupivacaine
- Ropivacaine
- Dibucaine (Cinchocaine)

### *Surface anaesthetic*

| *Soluble* | *Insoluble* |
|---|---|
| Cocaine | Benzocaine |
| Lidocaine | Butylaminobenzoate (Butamben) |
| Tetracaine | |
| Benoxinate | Oxethazaine |

Mepivacaine, Etidocaine, Articaine, Dyclonine, Proparacaine are other local anaesthetics, occasionally used in some countries.

Some other drugs, e.g. propranolol, chlorpromazine, $H_1$ antihistaminics, quinine have significant LA activity, but are not used for this purpose because of local irritancy or other prominent systemic activity. Local anaesthesia can be produced by cooling as well, e.g. application of ice, $CO_2$ snow, ethylchloride spray.

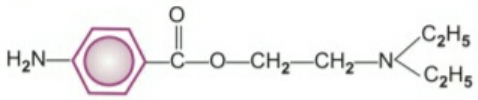
## CHEMISTRY

The clinically useful LAs are weak bases with amphiphilic property. A hydrophilic secondary

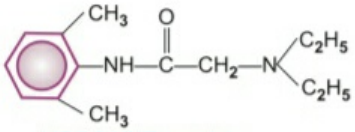
**TABLE 26.1** Comparative features of general and local anaesthesia

| | *General anaesthesia* | *Local anaesthesia* |
|---|---|---|
| 1. Site of action | CNS | Peripheral nerves |
| 2. Area of body involved | Whole body | Restricted area |
| 3. Consciousness | Lost | Unaltered |
| 4. Care of vital functions | Essential | Usually not needed |
| 5. Physiological trespass | High | Low |
| 6. Poor health patient | Risky | Safer |
| 7. Use in non-cooperative patient | Possible | Not possible |
| 8. Major surgery | Preferred | Cannot be used |
| 9. Minor surgery | Not preferred | Preferred |

or tertiary amine on one side and a lipophilic aromatic residue on the other are joined by an alkyl chain through an *ester* or *amide* linkage.



PROCAINE (ester)



LIDOCAINE (amide)

*Ester-linked LAs* Cocaine, procaine, chloroprocaine, tetracaine, benzocaine.

*Amide-linked LAs* Lidocaine, bupivacaine, dibucaine, prilocaine, ropivacaine.

**Features of amide LAs**
**(compared to ester LAs)**

- Produce more intense and longer lasting anaesthesia
- Bind to $\alpha_1$ acid glycoprotein in plasma
- Not hydrolysed by plasma esterases
- Rarely cause hypersensitivity reactions; no cross sensitivity with ester LAs

Because of their short duration, less intense analgesia and higher risk of hypersensitivity, the ester-linked LAs are rarely used for infiltration or nerve block, but are still used topically on mucous membranes.

## MECHANISM OF ACTION

The LAs block nerve conduction by decreasing the entry of $Na^+$ ions during upstroke of action potential (AP). As the concentration of the LA is increased, the rate of rise of AP and maximum depolarization decreases (Fig. 26.1) causing slowing of conduction. Finally, local depolarization fails to reach the threshold potential and conduction block ensues.

The LAs interact with a receptor situated within the voltage sensitive $Na^+$ channel and raise the threshold of channel opening: $Na^+$ permeability fails to increase in response to an impulse or stimulus. Impulse conduction is interrupted when the $Na^+$ channels over a critical length of the fibre (2–3 nodes of Ranvier in case of myelinated fibres) are blocked. The details are explained in Fig. 26.2. At physiological pH, the LA molecule is partly ionized. The equilibrium between the unionized base form (B) and the ionized cationic form ($BH^+$) depends on the pKa of the LA.

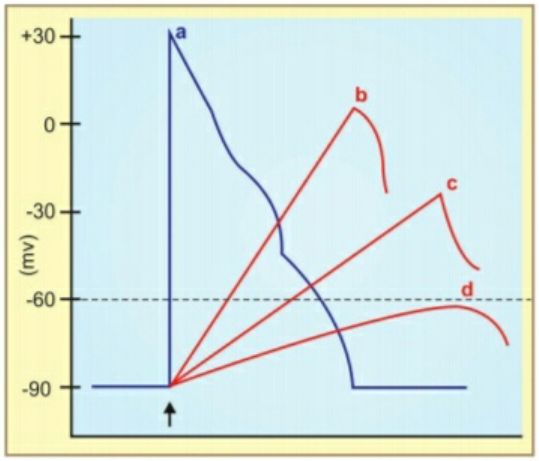



**Fig. 26.1:** Effect of progressively increasing concentrations (b,c,d) of a local anaesthetic on the generation of an action potential in a nerve fibre, (a) Untreated nerve fibre

Potency of a LA generally corresponds to the lipid solubility of its base form (B), because it is this form which penetrates the axon. However, the predominant active species is the cationic form of the LA which is able to approach its receptor only when the channel is open at the inner face, and it binds more avidly to the activated and inactivated states of the channel, than to the resting state. Binding of the LA prolongs the inactivated state. The channel takes longer to recover → refractory period of the fibre is increased. A resting nerve is rather resistant to blockade. Blockade develops rapidly when the nerve is stimulated repeatedly. The degree of blockade is frequency dependent: greater blockade occurs at higher frequency of stimulation. Moreover, exposure to higher concentration of $Ca^{2+}$ reduces inactivation of $Na^+$

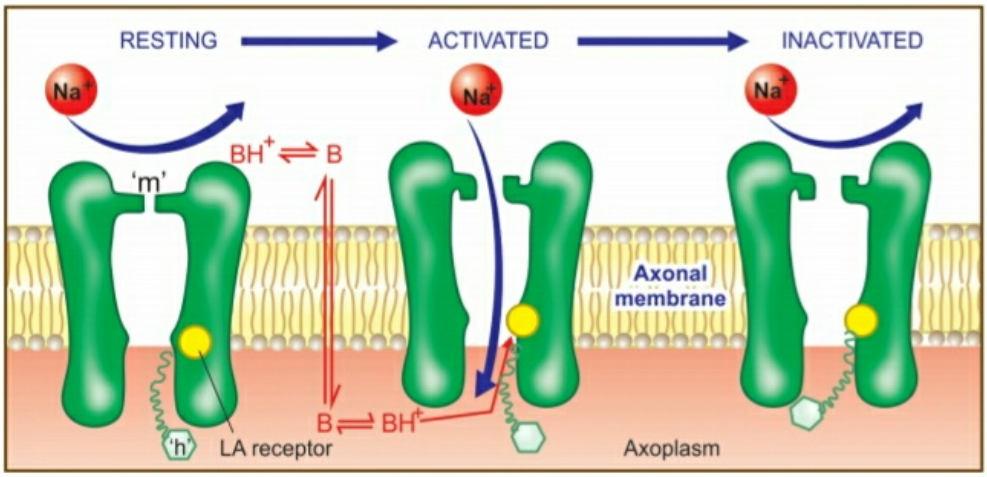



**Fig. 26.2:** A model of the axonal $Na^+$channel depicting the site and mechanism of action of local anaesthetics. The $Na^+$ channel has an activation gate (make or 'm' gate) near its extracellular mouth and an inactivation gate ( halt or 'h' gate) at the intracellular mouth. In the resting state the activation gate is closed. Threshold depolarization of the membrane opens the activation gate allowing $Na^+$ ions to flow in along the concentration gradient. Within a few msec, the inactivation gate closes and ion flow ceases. The channel recovers to the resting state in a time-dependent manner.

The local anaesthetic (LA) receptor is located within the channel in its intracellular half. The LA traverses the membrane in its unionized lipophilic form (B), reionizes in the axoplasm and approaches the LA receptor through the intracellular mouth of the channel. It is the cationic form ($BH^+$) of the LA which primarily binds to the receptor. The receptor has higher affinity, or is more accessible to the LA in the activated as well as inactivated states compared to the resting state. Binding of LA to its receptor stabilizes the channel in the inactivated state and thus reduces the probability of channel opening.

The neuronal $Na^+$ channel is a 300 KD glycoprotein composed of a large ($\alpha$) and two small ($\beta_1$, $\beta_2$) subunits. The $\alpha$ subunit encloses the $Na^+$ selective pore within its 4 homologous domains (I to IV), each domain has 6 membrane spanning helical segments (S1 to S6) connected alternately by intracellular and extracellular loops. The wall of the pore is formed by all four S5-S6 segments, while the short nonhelical loops connecting S5-S6 on the extracellular surface fold into the pore and serve as the activation gate. Voltage sensors located in the S4 segments move vertically on depolarization and open the activation gate by allosteric conformational change. A few msec later, the short intracellular loop connecting domains III and IV folds into the inner mouth of the pore inactivating the channel. The LA receptor is located in the S6 segment of domain IV. Channel activation either transforms the LA receptor to a higher affinity conformation or exposes it on the wall of the pore, and this persists during the subsequent inactivation phase.

channels and lessens the degree of block. Blockade of conduction by LA is not due to hyperpolarization; in fact, resting membrane potential is unaltered because $K^+$ channels are blocked only at higher concentrations of LA.

The onset time of blockade is related primarily to the pKa of the LA. Those with lower pKa (7.6–7.8), e.g. lidocaine, mepivacaine are fast acting, because 30–40% LA is in the undissociated base form at pH 7.4 and it is this form which penetrates the axon. Procaine, tetracaine, bupivacaine have higher pKa (8.1–8.9), only 15% or less is unionized at pH 7.4; these are slow acting. Chloroprocaine is an exception, having rapid onset despite high pKa (9.1).

## LOCAL ACTIONS

The clinically used LAs have no/minimal local irritant action and block sensory nerve endings, nerve trunks, neuromuscular junction, ganglionic synapse and receptors (non-selectively), i.e. those structures which function through increased $Na^+$ permeability. They also reduce release

of acetylcholine from motor nerve endings. Injected around a mixed nerve they cause anaesthesia of skin and paralysis of the voluntary muscle supplied by that nerve.

Sensory and motor fibres are inherently equally sensitive, but some LAs do exhibit unequal ability to block them, e.g. bupivacaine produces sensory block at much lower concentration than that needed for motor block. The sensitivity to LA is determined by diameter of the fibres as well as by fibre type. Diameter remaining the same, myelinated nerves are blocked earlier than nonmyelinated. In general, smaller fibres are more sensitive than larger fibres. Fibres differ in the critical length of the axon that must be exposed to the LA for effective blockade. Smaller fibres tend to have shorter critical lengths, because in them voltage changes propagate passively for shorter distances. Also, more slender axons have shorter internodal distances and LAs easily enter the axon at the nodes of Ranvier. The density of $Na^+$ channel is much higher at these nodes. Moreover, frequency dependence of blockade makes smaller sensory fibres more vulnerable since they generate high frequency longer lasting action potentials than the motor fibres. Thus, fibre diameter itself may not govern sensitivity to LA.

Autonomic fibres are generally more susceptible than somatic fibres. Among the somatic afferents order of blockade is: pain—temperature sense—touch—deep pressure sense. Since pain is generally carried by smaller diameter fibres than those carrying other sensations or motor impulses, pain in the first modality to be affected. Applied to the tongue, bitter taste is lost first followed by sweet and sour, and salty taste last of all.

In general, fibres that are more susceptible to LA are the first to be blocked and the last to recover. Also, location of the fibre within a nerve trunk determines the latency, duration and often the depth of local anaesthesia. Nerve sheaths restrict diffusion of the LA into the nerve trunk so that fibres in the outer layers are blocked earlier than the inner or core fibres. As a result, the more proximal areas supplied by a nerve are affected earlier because axons supplying them are located more peripherally in the nerve than those supplying distal areas. The differential arrangement of various types of sensory and motor fibres in a mixed nerve may partly account for the differential blockade. Motor fibres are usually present circumferentially; may be blocked earlier than the sensory fibres in the core of the nerve.

The LA often fails to afford adequate pain control in inflamed tissues (like infected tooth). The likely reasons are:

a. Inflammation lowers pH of the tissue—greater fraction of the LA is in the ionized form hindering diffusion into the axolemma.
b. Blood flow to the inflamed area is increased—the LA is removed more rapidly from the site.
c. Effectiveness of Adr injected with the LA is reduced at the inflamed site.
d. Inflammatory products may oppose LA action.

Addition of a vasoconstrictor, e.g. adrenaline (1:50,000 to 1:200,000):

- Prolongs duration of action of LAs by decreasing their rate of removal from the local site into the circulation: contact time of the LA with the nerve fibre is prolonged.
- Enhances the intensity of nerve block.
- Reduces systemic toxicity of LAs: rate of absorption is reduced and metabolism keeps the plasma concentration lower.
- Provides a more bloodless field for surgery.
- Increases the chances of subsequent local tissue edema and necrosis as well as delays wound healing by reducing oxygen supply and enhancing oxygen consumption in the affected area.
- May raise BP and promote arrhythmia in susceptible individuals.

## SYSTEMIC ACTIONS

Any LA injected or applied locally is ultimately absorbed and can produce systemic effects

depending on the concentration attained in the plasma and tissues.

### C.N.S.

All LAs are capable of producing a sequence of stimulation followed by depression. *Cocaine* is a powerful CNS stimulant causing in sequence euphoria—excitement—mental confusion—restlessness—tremor and twitching of muscles—convulsions—unconsciousness—respiratory depression—death, in a dose-dependent manner.

*Procaine* and other synthetic LAs are much less potent in this regard. At safe clinical doses, they produce little apparent CNS effects. Higher dose or accidental i.v. injection produces CNS stimulation followed by depression.

The early neurological symptoms of overdose with *lidocaine* and other clinically used LAs are—circumoral numbness, abnormal sensation in the tongue, dizziness, blurred vision, tinnitus followed by drowsiness, dysphoria and lethargy. Still higher doses produce excitation, restlessness, agitation, muscle twitching, seizures and finally unconsciousness.

The basic action of all LAs is neuronal inhibition; the apparent stimulation seen initially is due to inhibition of inhibitory neurones. At high doses, all neurones are inhibited and flattening of waves in the EEG is seen.

### C.V.S.

*Heart* LAs are cardiac depressants, but no significant effects are observed at conventional doses. At high doses (2–3 times the doses producing CNS effects) or on inadvertent i.v. injection, they decrease automaticity, excitability, contractility, conductivity and prolong effective refractory period (ERP). They have a quinidine-like antiarrhythmic action. *Procaine* is not used as antiarrhythmic because of short duration of action and propensity to produce CNS effects, but its amide derivative *procainamide* is a class IA antiarrhythmic (*see* Ch. 38). Electrophysiological properties of heart may be markedly altered at high plasma concentrations of LAs : QTc interval is prolonged and LAs can themselves induce cardiac arrhythmias. *Bupivacaine* is relatively more cardiotoxic and has produced ventricular tachycardia or fibrillation. *Lidocaine* has little effect on contractility and conductivity; it abbreviates ERP and has minimal proarrhythmic potential. It is used as an antiarrhythmic (*see* Ch. 38).

*Blood vessels* LAs tend to produce fall in BP. This is primarily due to sympathetic blockade, but high concentrations, as obtained locally at the site of injection, do cause direct relaxation of arteriolar smooth muscle. Bupivacaine is more vasodilatory than lidocaine, while prilocaine is the least vasodilatory. Toxic doses of LAs produce cardiovascular collapse. *Cocaine* has sympathomimetic property; increases sympathetic tone, causes local vasoconstriction, marked rise in BP and tachycardia.

Procaine and related drugs have weak anticholinergic, antihistaminic, ganglion blocking, neuromuscular blocking and smooth muscle relaxant properties, but these are clinically insignificant.

## PHARMACOKINETICS

Because LAs act near their site of administration, pharmacokinetic characteristics are not important determinants of their efficacy, but markedly influence their systemic effects and toxicity.

Soluble surface anaesthetics (lidocaine, tetracaine) are rapidly absorbed from mucous membranes and abraded areas, but absorption from intact skin is minimal. Procaine does not significantly penetrate mucous membranes. Rate of absorption depends on the blood flow to the area of application or injection. The absorbed LA being lipophilic is widely distributed; rapidly enters highly perfused brain, heart, liver, and kidney, followed by muscle and other viscera.

Procaine is negligibly bound to plasma proteins, but amide LAs are bound to plasma $\alpha_1$ acid glycoprotein. LAs are rapidly but temporarily bound to tissues, especially nerves, at the site of injection. Ester-linked LAs (procaine, etc.) are rapidly hydrolysed by plasma pseudocholinesterase and the remaining by esterases in the

liver. Amide-linked LAs (lidocaine, etc.) are degraded only in the liver microsomes by dealkylation and hydrolysis. Metabolism of lidocaine is hepatic blood-flow dependent. The maximal safe dose of LAs is lower in patients with hepatic disease and in the elderly who have decreased liver function.

After oral ingestion both procaine and lidocaine have high first pass metabolism in the liver. Thus, they are not active orally for anti-arrhythmic purposes.

## ADVERSE EFFECTS

Systemic toxicity on rapid i.v. injection is related to the intrinsic anaesthetic potency of the LA. However, toxicity after topical application or regional injection is influenced by the relative rates of absorption and metabolism. Those rapidly absorbed but slowly metabolized are more toxic.

(1) CNS effects are light-headedness, dizziness, auditory and visual disturbances, mental confusion, disorientation, shivering, twitchings, involuntary movements, finally convulsions and respiratory arrest. This can be prevented and treated by diazepam.

(2) Cardiovascular toxicity of LAs is manifested as bradycardia, hypotension, cardiac arrhythmias and vascular collapse.

(3) Injection of LAs may be painful, but local tissue toxicity of LAs is low. However, wound healing may be sometimes delayed. Addition of vasoconstrictors enhances the local tissue damage; rarely necrosis results. Vasoconstrictors should not be added for ring block of hands, feet, fingers, toes, penis and in pinna. Bupivacaine has the highest local tissue irritancy.

(4) Hypersensitivity reactions like rashes, angioedema, dermatitis, contact sensitization, asthma and rarely anaphylaxis occur. These are more common with ester-linked LAs, but rare with lidocaine or its congeners. Cross reactivity is frequent among ester compounds, but not with amide-linked LAs.

Often methylparaben added as preservative in certain LA solutions is responsible for the allergic reaction.

### Precautions and interactions

1. Before injecting the LA, aspirate lightly to avoid intravascular injection.
2. Inject the LA slowly and take care not to exceed the maximum safe dose, especially in children.
3. Propranolol (probably other β blockers also) may reduce metabolism of lidocaine and other amide LAs by reducing hepatic blood flow.
4. Vasoconstrictor (adrenaline) containing LA should be avoided for patients with ischaemic heart disease, cardiac arrhythmia, thyrotoxicosis, uncontrolled hypertension, and those receiving β blockers (rise in BP can occur due to unopposed α action) or tricyclic antidepressants (uptake blockade and potentiation of Adr).

## INDIVIDUAL COMPOUNDS

Important properties of local anaesthetics are compared in Table 26.2.

**Cocaine** It is a natural alkaloid from leaves of *Erythroxylon coca*, a south American plant growing on the foothills of the Andes. The natives of Peru and Bolivia habitually chew these leaves. Cocaine is a good surface anaesthetic and is rapidly absorbed from buccal mucous membrane. It was first used for ocular anaesthesia in 1884. Cocaine should never be injected; it is a protoplasmic poison and causes tissue necrosis. Cocaine produces prominent CNS stimulation with marked effect on mood and behaviour. It induces a sense of wellbeing, delays fatigue and increases power of endurance. In susceptible individuals it produces a state referred to as 'high' leadting to strong psychological but little physical dependence. Cocaine is unique among drugs of abuse in not producing significant tolerance on repeated use; sometimes reverse tolerance is seen (behavioural effects are experienced at lower doses).

Cocaine also stimulates vagal centre→bradycardia; vasomotor centre→rise in BP; vomiting centre→nausea and vomiting; temperature regulating centre→pyrexia (also due to increased heat production as a result of enhanced muscular activity).

In the periphery, it blocks uptake of NA and Adr into adrenergic nerve endings, (*see* Fig. 9.4) resulting in higher concentration of the transmitter around the receptors→ sympathomimetic effect, potentiation of directly acting sympathomimetics and suppression of indirectly acting sympathomimetics. Local vasoconstriction, tachycardia, rise in BP and mydriasis are the manifestations of its sympathomimetic action.

**TABLE 26.2 Comparative properties of important local anaesthetics**

| | Potency | | | Concn. used | Safe max* dose (inj.) | | Onset of action | Metabolism in | | Duration of nerve block (min.) |
|---|---|---|---|---|---|---|---|---|---|---|
| | surface | injection | toxic | | Total (mg) | (mg/kg) | | plasma | liver | |
| Cocaine | 1 | 1 | 1 | – | not injected | | fast | – | + | – |
| Procaine | 1/10 | 1/2 | 1/6 | 1–2% | 400 (6) | | slow | + | + | 30–60 |
| Lidocaine | 1 | 2 | 1/6 | 0.5–2% | 300 (4.5) | | fast | – | + | 60–120 |
| Tetracaine | 4 | 10 | 2 | 0.25–0.5% | 80 (1.2) | | slow | + | + | 180–480 |
| Bupivacaine | – | 10 | 2 | 0.25–0.5% | 100 (1.5) | | interm. | – | + | 120–360 |
| Dibucaine | 6 | 15 | 3 | 0.25–0.5% | 50 | | slow | – | + | 180–600 |

* Without adrenaline; addition of adrenaline may increase safe limit by upto 40%

The only indication for cocaine is in ocular anaesthesia. However, it causes constriction of conjunctival vessels, clouding and rarely sloughing of cornea (due to drying and local tissue toxicity). Its use, therefore, is not warranted.

**Procaine** It is the first synthetic local anaesthetic introduced in 1905. Its popularity declined after the introduction of lidocaine, and it is not used now. It is not a surface anaesthetic.

Procaine forms poorly soluble salt with benzyl penicillin; *procaine penicillin* injected i.m. acts for 24 hours due to slow absorption from the site of injection.

**Lidocaine (Lignocaine)** Introduced in 1948, it is currently the most widely used LA. It is a versatile LA, good both for surface application as well as injection and is available in a variety of forms. Injected around a nerve it blocks conduction within 3 min, whereas procaine may take 15 min; also anaesthesia is more intense and longer lasting. Vasodilatation occurs in the injected area. It is used for surface application, infiltration, nerve block, epidural, spinal and intravenous regional block anaesthesia. Cross sensitivity with ester LAs is not seen. In contrast to other LAs, early central effects of lidocaine are depressant, i.e. drowsiness, mental clouding, dysphoria, altered taste and tinnitus. Overdose causes muscle twitching, convulsions, cardiac arrhythmias, fall in BP, coma and respiratory arrest like other LAs. Lidocaine is a popular antiarrhythmic (*see* Ch. 38)

XYLOCAINE, GESICAIN 4% topical solution, 2% jelly, 2% viscous, 5% ointment, 1% and 2% injection (with or without adrenaline), 5% heavy (for spinal anaesthesia); 100 mg/ml spray (10 mg per actuation).

A transdermal patch of lidocaine has been produced for application over the affected skin for relief of burning pain due to postherpetic neuralgia.

**Prilocaine** It is similar to lidocaine but does not cause vasodilatation at the site of infiltration and has lower CNS toxicity due to larger volume of distribution. One of its metabolites has potential to cause methaemoglobinaemia. It has been used mainly for infiltration, nerve block and intravenous regional anaesthesia.

**Eutectic lidocaine/prilocaine** This is a unique preparation which can anaesthetise intact skin after surface application. *Eutectic mixture* refers to lowering of melting point of two solids when they are mixed. This happens when lidocaine and prilocaine are mixed in equal proportion at 25°C. The resulting oil is emulsified into water to form a cream that is applied under occlusive dressing for 1 hr before i.v. cannulation, split skin graft harvesting and other superficial procedures. Anaesthesia up to a depth of 5 mm lasts for 1–2 hr after removal. It has been used as an alternative to lidocaine infiltration.

PRILOX 5% cream.

**Tetracaine (Amethocaine)** A highly lipid-soluble PABA ester, more potent and more toxic due to slow hydrolysis by plasma pseudocholinesterase. It is both surface and conduction block anaesthetic, but its use is restricted to topical application to the eye, nose, throat, tracheobronchial tree and rarely for spinal or caudal anaesthesia of long duration. Though it is slow acting, absorption from tracheobronchial

spray is very fast and blood concentrations approach those attained after i.v. injection.
ANETHANE powder for solution, 1% ointment.

**Bupivacaine** A potent and long-acting amide-linked LA: used for infiltration, nerve block, epidural and spinal anaesthesia of long duration. A 0.25–0.5% solution injected epidurally produces adequate analgesia without significant motor blockade. As a result, it has become very popular in obstetrics (mother can actively cooperate in vaginal delivery) and for postoperative pain relief by continuous epidural infusion. It has high lipid-solubility; distributes more in tissues than in blood after spinal/epidural injection. Therefore, it is less likely to reach the foetus (when used during labour) to produce neonatal depression. Bupivacaine is more prone to prolong QTc interval and induce ventricular tachycardia or cardiac depression—should not be used for intravenous regional analgesia. Epidural anaesthesia with 0.75% bupivacaine during labour has caused few fatalities due to cardiac arrest; use of this concentration is contraindicated.
MARCAIN 0.5%, 1% (hyperbaric for spinal anaesthesia).
SENSORCAINE 0.25%, 0.5% inj, 0.5% heavy inj.
The S(–) enantiomer *Levobupivacaine* is equally potent but less cardiotoxic and less prone to cause seizures (after inadvertant intravascular injection) than racemic bupivacaine. It has been introduced in some countries as a single enantiomer preparation.

**Ropivacaine** A newer bupivacaine congener, equally long acting but less cardiotoxic. It blocks Aδ and C fibres (involved in pain transmission) more completely than Aβ fibres which control motor function. Though equieffective concentrations of ropivacaine are higher than those of bupivacaine, a greater degree of separation between sensory and motor block has been obtained with epidural ropivacaine. Continuous epidural ropivacaine is being used for relief of postoperative and labour pain. It can also be employed for nerve blocks. Recently, it has been approved for use in India.

**Dibucaine (Cinchocaine)** It is the most potent, most toxic and longest acting LA. It is used as a surface anaesthetic on less delicate mucous membranes (anal canal). Use for spinal anaesthesia of long duration has declined after the availability of bupivacaine.
NUPERCAINE 0.5% inj., NUPERCAINAL 1% ointment, in OTOGESIC 1% ear drops.

**Benoxinate** It is a good surface anaesthetic for the eye; has little irritancy. A 0.4% solution rapidly produces corneal anaesthesia sufficient for tonometry without causing mydriasis or corneal damage.
BENDZON 0.4% eyedrops.

**Benzocaine and Butylaminobenzoate (Butamben)** Because of very low aqueous solubility, these LAs are not significantly absorbed from mucous membranes or abraded skin. They produce long-lasting anaesthesia without systemic toxicity. They are used as lozenges for stomatitis, sore throat; as dusting powder/ointment on wounds/ulcerated surfaces and as suppository for anorectal lesions. Both are PABA derivative—can antagonize sulfonamides locally.
PROCTOSEDYL-M: Butylaminobenzoate 1% oint with framycetin and hydrocortisone acetate: for piles.
PROCTOQUINOL 5% ointment of benzocaine. ZOKEN 20% gel.

**Oxethazaine** A potent topical anaesthetic, unique in ionizing to a very small extent even at low pH values. It is, therefore, effective in anaesthetising gastric mucosa despite acidity of the medium. Swallowed along with antacids it affords symptomatic relief in gastritis, drug induced gastric irritation, gastroesophageal reflux and heartburn of pregnancy. Doses exceeding 100 mg/day may produce dizziness and drowsiness.
MUCAINE 0.2% in alumina gel + magnesium hydroxide suspension; 5–10 ml orally.
TRICAINE-MPS: Oxethazaine 10 mg with methyl polysiloxane 125 mg, alum. hydroxide gel 300 mg, mag. hydroxide 150 mg per 5 ml gel.

## USES AND TECHNIQUES OF LOCAL ANAESTHESIA

**1. Surface anaesthesia** It is produced by topical application of a surface anaesthetic to mucous membranes and abraded skin. Only the superficial layer is anaesthetised and there is no loss of motor function. Onset and duration depends on the site, the drug, its concentration and form, e.g. lidocaine (10%) sprayed in the throat acts in 2–5 min and produces anaesthesia for 30–45 min. Addition of Adr does not affect duration of topical anaesthesia, but phenylephrine can cause mucosal vasoconstriction and prolong topical anaesthesia. Absorption of soluble LAs from mucous membranes is rapid; blood concentrations of lidocaine and tetracaine

sprayed in throat/tracheobronchial tree approach those attained on i.v. injection—toxicity can occur. Except for eutectic lidocaine/prilocaine, no other LA is capable of anaesthetizing intact skin. The sites and purposes for which surface anaesthesia is used are given in Table 26.3.

**2. Infiltration anaesthesia** Dilute solution of LA is infiltrated under the skin in the area of operation—blocks sensory nerve endings. Onset of action is almost immediate and duration is shorter than that after nerve block, e.g. lidocaine 30–60 min, bupivacaine 90–180 min. Infiltration is used for minor operations, e.g. incisions, excisions, hydrocele, herniorrhaphy, etc. when the area to be anaesthetised is small. Relatively larger amount of LA is required compared to the area anaesthetized, but motor function is not affected.

**3. Conduction block** The LA is injected around nerve trunks so that the area distal to injection is anaesthetised and paralysed. Choice of the LA and its concentration is mainly dictated by the required duration of action; lidocaine (1–2%) with intermediate duration of action is most commonly used, but for longer lasting anaesthesia bupivacaine may be selected.

(a) *Field block* It is produced by injecting the LA subcutaneously in a manner that all nerves coming to a particular field are blocked—as is done for herniorrhaphy, appendicectomy, dental procedures, scalp stitching, operations on forearms and legs, etc. Larger area beginning 2–3 cm distal to the line of injection can be anaesthetised with lesser drug compared to infiltration. The same concentration of LA as for infiltration is used for field block.

(b) *Nerve block* It is produced by injecting the LA around the appropriate nerve trunks or plexuses. The area of resulting anaesthesia is still larger compared to the amount of drug used. Muscles supplied by the injected nerve/plexus are paralysed. The latency of anaesthesia depends on the drug and the area to be covered by diffusion, e.g. lidocaine anaesthetises intercostal nerves within 3 min, but brachial plexus block may take 15 min. For plexus block a 'flooding'

**TABLE 26.3 Sites and uses of surface anaesthesia**

| *Site* | *Drugs* | | *Form* | *Purpose* |
|---|---|---|---|---|
| 1. Eye | Tetracaine<br>Benoxinate | 1–2%<br>0.4% | ointment, drops<br>drops | tonometry, surgery<br>tonometry |
| 2. Nose, ear | Lidocaine<br>Tetracaine | 2–4%<br>1–2% | drops | painful lesions, polyps |
| 3. Mouth, throat | Benzocaine<br>Lidocaine | <br>2% | lozenges<br>rinse solution | stomatitis, sore throat<br>painful ulcers |
| 4. Pharynx, larynx, trachea, bronchi | Lidocaine<br>Tetracaine | 4–10%<br>1–2% | spray | tonsillectomy, endotracheal intubation, endoscopies |
| 5. Esophagus, stomach | Oxethazaine | 0.2% | suspension<br>heartburn | gastritis, esophagitis, |
| 6. Abraded skin | Tetracaine<br>Benzocaine<br>Butamben | 1%<br>1–2%<br>1–2% | cream, ointment, dusting powder | ulcers, burns, itching dermatoses |
| 7. Intact skin | Eutectic lidocaine/ prilocaine | 5% | cream under occlusion | i.v. cannulation, skin surgery |
| 8. Urethra | Lidocaine | 2% | jelly | for dilatation, catheterisation |
| 9. Anal canal, rectum | Lidocaine<br>Dibucaine<br>Benzocaine | 4%<br>1%<br>5% | ointment, cream, suppository | fissure, painful piles, surgery, proctoscopy |

technique is used and larger volumes are needed. Nerve block lasts longer than field block or infiltration anaesthesia. Frequently performed nerve blocks are—lingual, intercostal, ulnar, sciatic, femoral, brachial plexus, trigeminal, facial, phrenic, etc.—used for tooth extraction, operations on eye, limbs, abdominal wall, fracture setting, trauma to ribs, neuralgias, persistent hiccup, etc.

The primary purpose of nerve block anaesthesia is to abolish pain and other sensations. The accompanying motor paralysis may be advantageous by providing muscle relaxation during surgery, as well as disadvantageous if it interferes with breathing, ability to walk after the operation, or participation of the patient in labour or produces postural hypotension.

**4. Spinal anaesthesia** The LA is injected in the subarachnoid space between L2–3 or L3–4 i.e. below the lower end of spinal cord. The primary site of action is the nerve roots in the cauda equina rather than the spinal cord. Lower abdomen and hind limbs are anaesthetised and paralysed. The level of anaesthesia depends on the volume and speed of injection, specific gravity of drug solution and posture of the patient. The drug solution could be hyperbaric (in 10% glucose) or isobaric with CSF.

Nerve roots rapidly take up and retain the LA, therefore, its concentration in CSF falls quickly after injection. The level of anaesthesia does not change with change of posture (becomes fixed) after 10 min. Also, higher segments are exposed to progressively lower concentrations of the LA. Since autonomic preganglionic fibres are more sensitive and somatic motor fibres less sensitive than somatic sensory fibres, the level of sympathetic block is about 2 segments higher and the level of motor paralysis about 2 segments lower than the level of cutaneous analgesia.

The duration of spinal anaesthesia depends on the drug used and its concentration. Addition of 0.2–0.4 mg of adrenaline to the LA prolongs spinal anaesthesia by about 1/3rd when measured by the time taken for the level of sensory block to recede to L1. Adr may be enhancing spinal anaesthesia by reducing spinal cord blood flow or by its own analgesic effect exerted through spinal $\alpha_2$ adrenoceptors (intrathecal clonidine, an $\alpha_2$ agonist, produces spinal analgesia by itself).

**TABLE 26.4** Drugs used for spinal anaesthesia and their duration of action

| Drug | Concentration (%) | Volume (ml) | Total dose (mg) | Duration of action (min) |
|---|---|---|---|---|
| Lidocaine | 1.5–5 | 1–2 | 25–100 | 60–90 |
| Bupivacaine | 0.5–0.75 | 2–3 | 10–25 | 90–150 |
| Tetracaine | 0.25–0.5 | 1–3 | 5–15 | 90–180 |

Women during late pregnancy require less drug for spinal anaesthesia, because inferior vena cava compression leads to engorgement of the vertebral system and a decrease in the capacity of subarachnoid space.

Spinal anaesthesia is used for operations on the lower limbs, pelvis, lower abdomen, e.g. prostatectomy, fracture setting, obstetric procedures, caesarean section, etc. Choice of the LA for spinal anaesthesia primarily depends on the nature and duration of the operative procedure. The LAs employed with their doses and duration of anaesthesia are given in Table 26.4.

Advantages of spinal anaesthesia over general anaesthesia are:

(i) It is safer.
(ii) Produces good analgesia and muscle relaxation without loss of consciousness.
(iii) Cardiac, pulmonary, renal disease and diabetes pose less problem.

### Complications of spinal anaesthesia

1. *Respiratory paralysis* with proper care, this is rare; intercostal muscles may be paralysed, but diaphragm (supplied by phrenic nerve) maintains breathing. Hypotension and ischaemia of respiratory centre is more frequently the cause of respiratory failure than diffusion of the anaesthetic to higher centres. Due to paralysis of external abdominal and intercostal muscles, coughing and expectoration becomes less effective. This may lead to pulmonary complications.

2. *Hypotension* It is due to blockade of sympathetic vasoconstrictor outflow to blood vessels; venous pooling and decreased return to the heart contributes more to the fall in BP than arteriolar dilatation. Paralysis of skeletal muscles of lower limb is another factor reducing venous return. Decreased sympathetic flow to heart and low venous return produce bradycardia. Raising the foot end overcomes the hypotension by promoting venous drainage. Sympathomimetics, especially those with prominent constrictor effect on veins (ephedrine, mephentermine) effectively prevent and counteract hypotension.

3. *Headache* is due to seepage of CSF; can be minimised by using smaller bore needle.

4. *Cauda equina syndrome* is a rare neurological complication resulting in prolonged loss of control over bladder and bowel sphincters. It may be due to traumatic damage to nerve roots or chronic arachnoiditis caused by inadvertent introduction of the antiseptic or particulate matter in the subarachnoid space.

5. *Septic meningitis* This may occur due to infection introduced during lumbar puncture. Actual incidence is very low in majority of hospitals.

6. *Nausea and vomiting* after abdominal operations is due to reflexes triggered by traction on abdominal viscera. Premedication with opioid analgesics prevents it.

**5. Epidural anaesthesia** The spinal dural space is filled with semiliquid fat through which nerve roots travel. The LA injected in this space—acts primarily on nerve roots (in the epidural as well as subarachnoid spaces to which it diffuses) and small amount permeates through intervertebral foramina to produce multiple paravertebral blocks. Epidural anaesthesia can be divided into 3 categories depending on the site of injection.

(i) *Thoracic* Injection is made in the midthoracic region. The epidural space in this region is relatively narrow, smaller volume of drug is needed and a wide segmental band of analgesia involving the middle and lower thoracic dermatomes is produced. It is used generally for pain relief following thoracic/upper abdominal surgery. Specially designed catheters are available which can be placed for repeated injections or continuous infusion of the LA to achieve epidural analgesia lasting few days.

**Contraindications to spinal anaesthesia**

- Hypotension and hypovolemia.
- Uncooperative or mentally ill patients.
- Infants and children—control of level is difficult.
- Bleeding diathesis.
- Raised intracranial pressure.
- Vertebral abnormalities e.g. kyphosis, lordosis, etc.
- Sepsis at injection site.

(ii) *Lumbar* Relatively large volume of drug is needed because epidural space is wide. It produces anaesthesia of lower abdomen, pelvis and hind limbs. Use of lumbar epidural anaesthesia is similar to that of spinal anaesthesia.

(iii) *Caudal* Injection is given in the sacral canal through the sacral hiatus—produces anaesthesia of pelvic and perineal region. It is used mostly for vaginal delivery, anorectal and genitourinary operations.

Lidocaine (1–2%) and bupivacaine (0.25–0.5%) are popular drugs for epidural anaesthesia. Onset is slower and duration of anaesthesia is longer with bupivacaine and action of both the drugs is prolonged by addition of adrenaline. Technically epidural anaesthesia is more difficult than spinal anaesthesia and relatively larger volumes of drug are needed. Consequently, blood concentrations of the LA are higher. Cardiovascular complications are similar to that after spinal anaesthesia, but headache and neurological complications are less likely, because intrathecal space is not entered. Spread of the LA in the epidural space is governed by the volume injected: larger volume anaesthetizes more extensive area. Zone of differential sympathetic blockade is not evident after epidural

injection but motor paralysis is 4–5 segments caudal, especially with lower concentrations of the drug. Greatest separation between sensory and motor block is obtained by use of 0.25% bupivacaine. This is especially valuable for obstetric purposes (mother can participate in labour without feeling pain) and for postoperative pain relief.

**6. Intravenous regional anaesthesia (Intravascular infiltration anaesthesia)** It consists of injection of LA in a vein of a tourniquet occluded limb such that the drug diffuses retrograde from the peripheral vascular bed to nonvascular tissues including nerve endings. The limb is first elevated to ensure venous drainage by gravity and then tightly wrapped in an elastic bandage for maximal exsanguination. Tourniquet is then applied proximally and inflated to above arterial BP. Elastic bandage is now removed and 20–40 ml of 0.5% lidocaine is injected i.v. under pressure distal to the tourniquet. Regional analgesia is produced within 2–5 min and lasts till 5–10 min after deflating the tourniquet which is kept inflated for not more than 15–60 min to avoid ischaemic injury. Deflation in < 15 min may allow toxic amounts of the LA to enter systemic circulation. The safety of the procedure depends on the rapid uptake of LA by peripheral tissues; only 1/4 of the injected drug enters systemic circulation when the tourniquet is released. Bradycardia can occur.

It is mainly used for the upper limb and for orthopedic procedures. Obstructing the blood supply of lower limb is more difficult and larger volume of anaesthetic is needed. Therefore, it is rarely used for lower limb, except the foot. Bupivacaine should not be employed because of its higher cardiotoxicity.

## PROBLEM DIRECTED STUDY

**26.1** A healthy full-term primigravida aged 26 years who has gone into labour presents for delivery. There is no cephalopelvic disproportion or any other contraindication to normal vaginal delivery. However, she demands relief of pain associated with labour and delivery.

(a) Can some form of regional anaesthesia be used to relieve her pain? If so, which type of regional anaesthesia with which drug would be most suitable for her?

(see Appendix-1 for solution)