

Local Anesthetics

Site of Action / Mechanism / Effect	Options	Clinical Use	Ocular Side Effects	Systemic Side Effects	Differences between LAs	Contraindications Drug Interactions
<p><b>1. blocks Na channels</b> -prevent depolarization and action potentials in neural tissues -sensitivity related to fiber size, myelination, firing rate, activity</p> <p><b>2. block substance P release</b> -<math>\alpha_2</math> agonists -less sensitive to pain</p> <p><i>Step 1:</i> -entry nerve via a) <i>diffusion</i> (hydrophobic, unionized) b) <i>Na channels</i> (hydrophilic, ionized; bind better in "inactive" state) <i>Step 2:</i> -interact with Na channel proteins → unselective to nerve fibers, but selective based on size, myelination</p> <p><u>Requirements:</u> -ampiphilic -pH dependent 1. lipophilic aromatic ring 2. hydrophilic 2ndy/3ry/4ry amine 3. ester (short lived, topical) or amide (long acting, injectable) link via alkyl chain</p>	<p><u>Topical</u> (esters) <b>1. cocaine</b> -ester of benzoic acid -most toxic to cornea <b>2. propariacaine</b> -ester of meta-aminobenzoic acid <b>3. benoxinate</b> -oxybuprocaine -ester of para-aminobenzoic acid -least toxic to cornea <b>4. tetracaine</b> -pontacaine, ester of para-aminobenzoic acid, amethocaine -most toxic to cornea</p> <p><u>Injectable</u> (<i>tend to be amides</i>) <b>1. procaine (short acting)</b> -novacaine -ester of para-aminobenzoic acid <b>2. chlorprocaine</b> -ester of para-aminobenzoic acid <b>3. lidocaine</b> -lignocaine (<i>short acting</i>) -zylocaine -amide -myotoxicity problem <b>4. buprivacaine (long acting)</b> -amide -binds strongly to proteins <b>5. mepivacaine (intermediate duration of action)</b> -amide <b>6. etidocaine (long acting)</b> -amide -binds strongly to proteins</p> <p>Injectable: -combination LAs (short + long) -LA and vasoconstrictor</p>	<p><u>Topical</u> -tonometry -gonioscopy -foreign body removal -modified Schirmer test -corneal epithelial debridement -anterior segment surgery -enhanced mydriasis -forced duction -electrophysiology -lacrimial lavage?</p> <p><u>Injectable</u> <i>Regional anesthesia</i> -correction of lid postural problems/repairs -removal of "growths" -cataract surgery -refractive surgery</p> <p><i>Intracameral injection</i> -dilation effect</p>	<p><b>1. mild-severe corneal epithelial desquamation</b> -esp. cocaine &amp; tetracaine -benoxinate least -inhibits metabolism, decreases cell mitosis/migration, slows healing, disrupts tear layer and fundus view, facilitates debridement, improves corneal absorption of drugs</p> <p><b>2. myotoxicity problem</b> -lidocaine</p>	<p><u>Allergic reactions:</u></p> <p><i>Local</i> -onset of 5-10 min -increase with repeated exposure -conjunctival edema, hyperemia edematous lids, lacrimation</p> <p><i>Systemic</i> -increased risk with injection Urticaria, angioneurotic edema, bronchospasm, hypotension -anaphylactic reactions rare</p> <p><u>Due to Na channel blockade:</u> <b>1. block neuronal tissues</b> <b>2. inhibit CNS sites</b> → drowsiness, restlessness, convulsions, resp.depression, skeletal muscle tremor, HA <b>3. inhibit sympathetic fibers</b> <b>4. block cardiac muscle</b> (bupivacaine) → myocardial depression, cardiac arrest <b>5. block vascular smooth muscle</b> → hypotension <b>6. block other smooth muscles like the iris</b></p>	<p><b>1. penetration</b> -determines rate of onset; more lipophilic drugs have shorter onset; favored by alkaline pH -inhibited by inflammation b/c acidic</p> <p><b>2. metabolism rate</b> -affects duration a) esters -metabolized by esterases, short duration of action b) amides -metabolized in liver by P450, longer duration</p> <p><b>3. Protein Binding</b> -reduces active drug; may need higher dose -prolongs duration of action</p> <p><b>4. secondary vasodilation</b> -increases drug clearance and decreases duration → vasoconstrictor combos (e.g. phenylephrine, epinephrine)</p> <p><b>5. potency</b> -more lipid soluble drugs more potent -no gain with combos -minimal effect on lid margins</p>	<p>-other local anesthetics (e.g. benzocaine)</p> <p>-allergic cross reactivity (e.g. benoxinate with para-aminobenzoate drugs)</p> <p>-sulfonamides</p> <p>-interactions with drugs sharing secondary actions a) cocaine/adrenergic agonists (e.g. MAOIs, TCAs, methyropa, phenylephrine) → cumulative effect b) LAs/beta blockers with MSA → cumulative effect</p> <p>-interactions with enzyme inhibitors (ester drugs &amp; anticholinesterases)</p>

Opioids

Site of Action / Mechanism / Effect	Options	Clinical Use	Ocular Side Effects	Systemic Side Effects	Issues	Contraindications Drug Interactions
<p><b>1. decrease cAMP</b> -site of tolerance -linked to inhibitory G-protein</p> <p><b>2. decrease excitability</b> -open K<sup>+</sup> channels</p> <p><b>3. decrease transmitter release</b> -block Ca<sup>2+</sup> channels</p> <p>→ decrease activity in sensory nerves</p> <p><u>μ (supraspinal) &amp; κ (spinal) receptors</u> -analgesia (spinal, brain stem) -euphoria (limbic area)</p> <p><u>σ receptors</u> -dysphoria -hallucinations</p>	<p><u>mild-moderate pain</u></p> <p><b>1. codeine</b> μ -converted to heroin</p> <p><b>2. (di)hydrocodone</b> -more potent than codeine</p> <p><b>3. oxycodone</b> -more potent than codeine</p> <p><b>4. propoxyphene</b> -weak analgesic -for mild pain w/o much addiction risk</p> <p><u>moderate to severe pain (acute/chronic)</u></p> <p><b>1. heroin</b> μ <b>2. morphine</b> μ -converted to heroin</p> <p><b>3. methadone</b> <b>4. meperidine</b> <b>5. fentanyl</b> μ -80x more potent than morphine—very potent!! -anesthesia</p> <p><b>6. pentazocine</b> κ -mixed receptor actions -anesthesia</p> <p><b>7. buprenorphine</b> -mixed receptor actions -anesthesia</p> <p><b>8. buprenorphine</b> -anesthesia</p> <p><b>9. tramadol</b> -mixed actions -anesthesia -blocks serotonin uptake to be an indirect agonist; doesn't have to be as potent has opiod agonist to have same effect</p> <p><b>10. remifentanil</b> -short duration -anesthesia</p> <p><u>cough suppressant</u></p> <p><b>1. dextromethorphan</b> <b>2. pholcodine</b></p> <p><u>heroin addiction</u></p> <p><b>1. methadone</b> -agonists to substitute for heroin</p>	<p>1. mild, moderate to severe pain</p> <p>2. analgesia + CNS effects (euphoria, calming)</p>	<p>-pupil constriction (diagnostic aid) effect is central in EWN</p>	<p>-drowsiness, sedation, dizziness</p> <p>-euphoria</p> <p>-respiratory depression</p> <p>-elevated CSF pressure</p> <p>-nausea, vomiting</p> <p>-constipation (GI)</p> <p>-urinary retention</p> <p>-immunosuppression</p> <p>-glistening dots in retinal blood vessels from heroin</p>	<p><u>Tolerance</u> -12-24 hr to emesis, analgesia -μ receptor mediated -but, no tolerance to pupil/GI effects!</p> <p><u>Dependence</u> -physiological &amp; psychological -cause of abuse -source of withdrawal symptoms -less abuse potential with cocaine</p> <p><u>Tx Heroin addiction</u> -methadone (agonist) substitutes for heroin -naltrexone (antagonist) to quit "cold turkey"</p> <p><u>Administration</u> oral/injection</p>	