






Pharmacology of drugs acting on the eye

- Main text
- Male slide
- Female slide
- Important
- Dr, notes
- Extra info

EDITING FILE



Objectives

-  Outline common routes of administration of drugs to the eye.
-  Discuss the pharmacokinetics of drugs applied topically to the eye.
-  Classify drugs used for treatment of disorders of the eye.
-  Elaborate on autonomic drugs, anti-inflammatory drugs & and drugs used for glaucoma.
-  Outline ocular toxicity of some drugs.

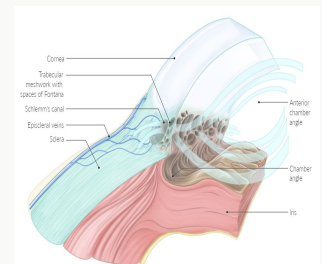
Autonomic Control of the Eye

	Parasympathetic N.S	Sympathetic N.S.
Iris	M_3 <u>Circular</u> muscles contract → <i>miosis</i>	α_1 <u>Radial</u> muscles contract → <i>mydriasis</i>
Ciliary muscle	M_3 Contracts → near vision (<i>accomodation</i>)	β_2 Relaxes → far vision
Lens	Thick, more convex	Thin, flattened
Suspensory Ligaments	Relax	Contract
Conjunctival B.V.	Vasodilation & congestion	Vasoconstriction & decongestion
Aqueous Humor		α_2 ↓ production β_2 ↑ production

Extra

Aqueous Humor

- Physiologically, **aqueous humor** is produced by the ciliary body by a combination of active transport of ions & ultrafiltration of interstitial fluid. The fluid flows from the posterior chamber over the surface of the lens through the pupil into the anterior chamber, then flows through the trabecular meshwork into Schlemm's canal to collect in the scleral veins.
- Intraocular pressure (IOP)** is a balance between fluid synthesis & drainage. Any process that disrupts that balance may raise IOP and lead to optic nerve damage & visual impairment.

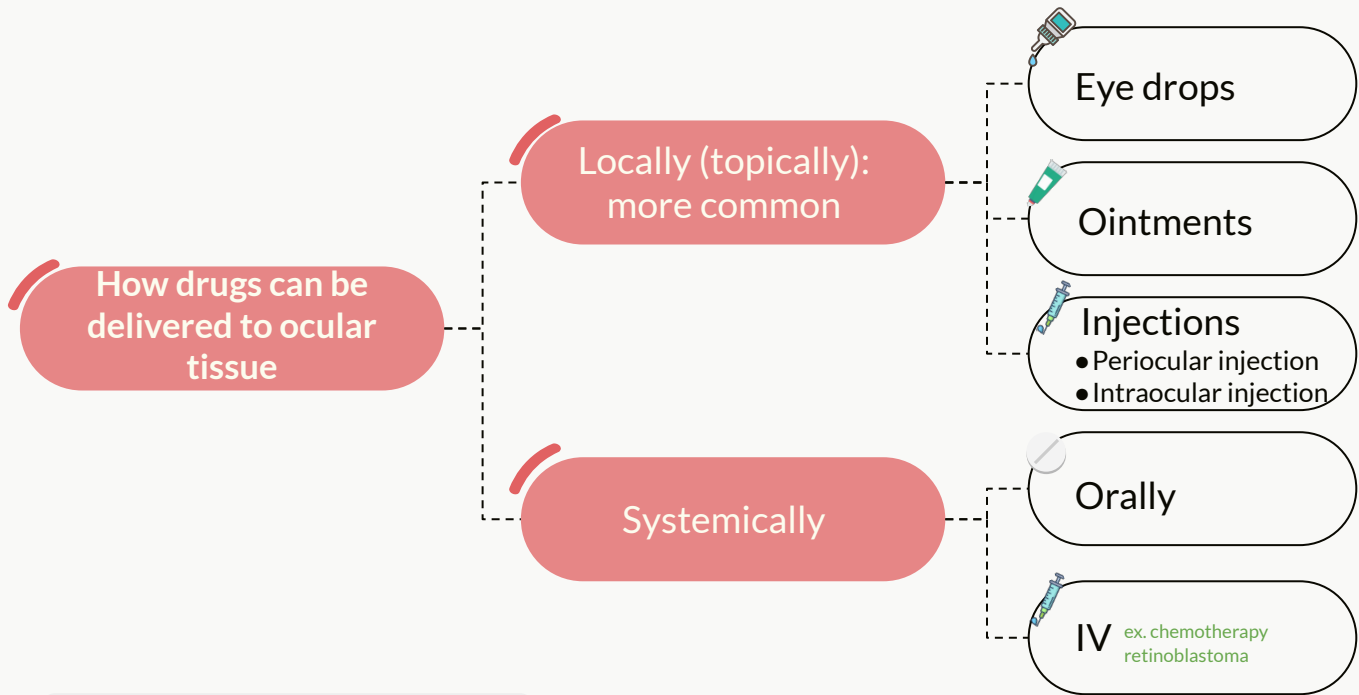


Glaucoma

-Glaucoma is a group of eye diseases characterized by progressive optic neuropathy that results in a specific pattern of irreversible optic disc changes & visual defects; frequently associated with ↑ IOP.

Open-angle Glaucoma	Closed-angle Glaucoma
A chronic condition of ↑ IOP due to slow clogging of Schlemm's canals with a wide-open angle. It leads to progressive (painless) visual field loss and, if left untreated, blindness.	An acute (painful) or chronic condition of ↑ IOP due to blockage of Schlemm's canal with a closed or narrow angle.
Eye drops that ↓ IOP by either of 2 mechanisms: <ul style="list-style-type: none"> ↓ Aqueous humor production ↑ Aqueous humor drainage 	An emergency ; initially managed with IOP-decreasing drugs that have a rapid onset of action, then patients <i>must</i> undergo procedure as soon as possible. *Avoid mydriatic drugs!

Routes of administration



Topical Drugs

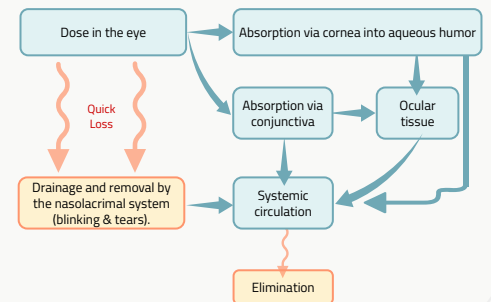
Rate of absorption is determined:

- **Drug residence time:** can be Prolonged by change of formulation.
- **Drug concentration and solubility:** higher the concentration better will be the penetration.

Viscosity: increases the contact time with the cornea.

Lipid solubility: higher the lipid solubility more will be the penetration

- **Metabolism :** esterases
- **Elimination by nasolacrimal drainage.**
- **Diffusion across cornea & conjunctiva.**

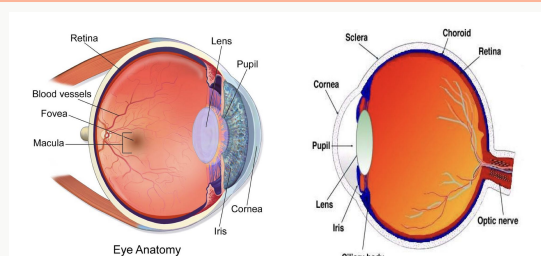


Systemic Drugs

Factors that can control systemic drug penetration into ocular tissue are:

- **lipid solubility of the drug:** more penetration with high lipid solubility
- **Protein binding:** more effect with low protein binding
- **Eye inflammation:** more penetration with ocular inflammation

Anatomy of the eye



Topical drugs

1- Eye drops

- Eye drops- most common .
- one drop = 50 μ l.
- Their contact time is low to be used several times.

2- Ointments

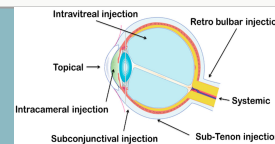
Advantages

- Increase the contact time of ocular medication to ocular surface thus better effect.

Disadvantages

- The drug has to be high lipid soluble to have the maximum effect.

3- Injections



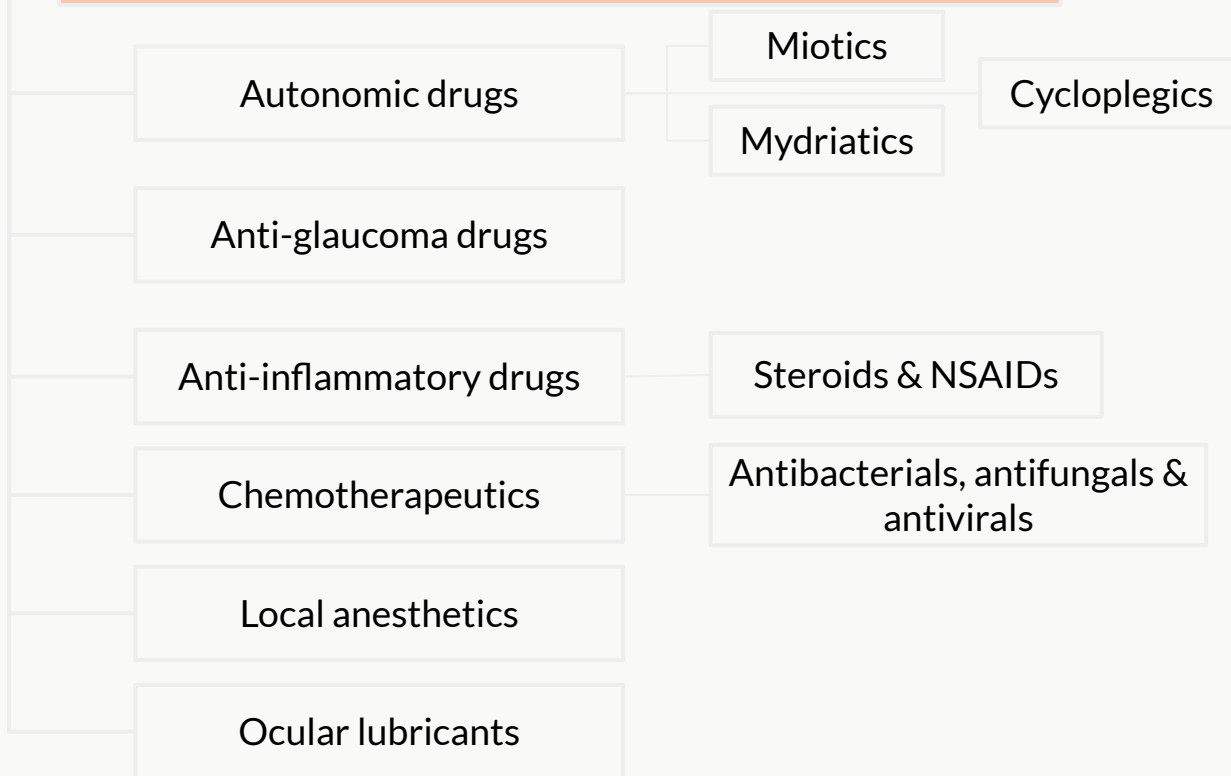
Intraocular Injections

	Intracameral	Intravitreal
Uses	<ul style="list-style-type: none"> • acetylcholine or lidocaine during cataract surgery 	<ul style="list-style-type: none"> • Antibiotics in cases of endophthalmitis • steroid in macular edema

Periocular injections

	Subconjunctival	retrobulbar	peribulbar
Uses	<ul style="list-style-type: none"> • reach behind iris-lens diaphragm better than topical application • For infection of anterior segment and inflammation of uvea • bypass the conjunctival and corneal epithelium which is good for drugs with low lipid solubility (e.g. penicillins) • Steroid and local anesthetics can be applied this way 		

Ocular drugs



Autonomic drugs- ocular actions

Parasympathetic Drugs (Cholinergic drugs)	Sympathetic Drugs (Adrenergic Drugs)
<ul style="list-style-type: none"> • Constriction of the pupillary sphincter muscle (miosis) 	<ul style="list-style-type: none"> • Contraction of dilator Pupillae (Active mydriasis) α_1
<ul style="list-style-type: none"> • Contraction of the ciliary muscle (accommodation for near vision). 	<ul style="list-style-type: none"> • Relaxation of ciliary muscles β_2
<ul style="list-style-type: none"> • Decrease in intraocular pressure \downarrow IOP. 	-
<ul style="list-style-type: none"> • increases aqueous outflow through the trabecular meshwork into canal of Schlemm by ciliary muscle contraction. 	<ul style="list-style-type: none"> • α & β receptors in the blood vessels of the ciliary processes \rightarrow help in regulation of aqueous humour formation.
<ul style="list-style-type: none"> • Increased lacrimation 	-
<ul style="list-style-type: none"> • Conjunctival Vasodilation 	<ul style="list-style-type: none"> • Vasoconstriction of conjunctival blood vessels α_1

Autonomic Drugs: *Parasympathetic*

Cholinergic Agonists

Direct Agonists

Agent	Methacholine	Carbachol	Pilocarpine
Uses	Induction of miosis in surgery		-
	Open-angle glaucoma		

Indirect-acting Agonists (Anticholinesterases)

Group	Reversible		irreversible	
Agent	Demecarium	Physostigmine	Isoflurophate	Ecothiophate
Uses	_____	<ul style="list-style-type: none"> • Glaucoma • Accommodative esotropia (Ecothiophate): occurs in far sighted patients who make huge effort to accommodate for near vision until their eyes get crossed to the opposite direction. 		

Both: Direct & Indirect

Uses	<ul style="list-style-type: none"> • Glaucoma (open & closed angle) mainly by ↑ drainage • Counteract action of mydriatics after fundoscopic examination • To break iris-lens adhesions → happens in inflammation and is treated by using drugs that cause contraction of iris muscle i.e. mydriatics & miotics
Ocular ADRs	<ul style="list-style-type: none"> • Diminished vision (myopia) • Headache

Autonomic Drugs: *Parasympathetic*

Cholinergic Antagonists (Muscarinic)

	Natural Alkaloids		Synthetic Atropine Substitutes		
Agent	Atropine	Scopolamine (Hyoscine)	Homatropine	Cyclopentolate	Tropicamide
D.O.A.	7-10 days (long duration of action)	3-7 days	1-3 days	24 h	6 h
	What is the difference between natural alkaloids & synthetic atropine? duration of action				
Action	<ul style="list-style-type: none"> ● Passive mydriasis due to relaxation of circular muscles ● Cycloplegia (loss of near accommodation) due to relaxation of ciliary muscles ● ↑ IOP ● Loss of light reflex ● ↓ Lacrimal secretion → sandy eye 				
Uses	<ul style="list-style-type: none"> ● Funduscopy examination of the eye especially those with short DOA. ● To prevent adhesion of iris to lens in uveitis & iritis → here sympathomimetic drugs, parasympathomimetic drugs & muscarinic antagonist can be used [439]. ● Measurement of refractive error (myopia, hyperopia). ● Sometimes use atropine in case lazy eye (growth of one eye will be less than other eye and that cause vision problems) 				
C.I	Glaucoma (especially closed-angle)				

Autonomic Drugs: Sympathetic

Adrenergic Agonists

Group	Selective α_2	Selective α_1	Non-selective ($\alpha_{1\&2}$ $\beta_{1\&2}$)
Agent	Apraclonidine (eye drops) <i>sympatholytic</i>	Phenylephrine	Epinephrine & its pro-drug "Dipivefrin"
M.O.A.	<ul style="list-style-type: none"> • ↓ Aqueous humor production • ↑ Uveoscleral outflow of aqueous humor 	<ul style="list-style-type: none"> • Active mydriasis by contraction of radial muscles (without cycloplegia). • No effect on accommodation. 	<ul style="list-style-type: none"> • ↓ Aqueous humor production by constriction of ciliary B.V. • ↑ Uveoscleral outflow of aqueous humor
Uses	<ul style="list-style-type: none"> • Open-angle glaucoma • Prophylaxis against IOP spiking after glaucoma • laser procedures. 	<ul style="list-style-type: none"> • Fundoscopic examination of eye. • To prevent adhesion in uveitis & iritis. • Ocular decongestant in minor allergic hyperemia of eye (by vasoconstriction). 	Used locally as eye drops in open-angle glaucoma
ADRs	<ul style="list-style-type: none"> • Hypotension • Headache • Bradycardia 	<ul style="list-style-type: none"> • May cause significantly ↑ B.P. • Rebound congestion 	<ul style="list-style-type: none"> • ↑ B.P. • Headache • Arrhythmia
C.I	CVS patients	Precipitation of closed-angle glaucoma in patients with narrow angles	

β Blockers

Group	Selective β ₁ (Cardioselective)	Non-selective	
Agent	<u>Betaxolol</u>	<u>Carteolol</u>	<u>Timolol</u>
M.O.A.	Act on ciliary body to ↓ production of aqueous humor.		
P.K.	Given topically as eye drops.		
Pros	<ul style="list-style-type: none"> • Can be used in patients with hypertension. • Betaxolol: does not cause bronchospasm. 		
Uses	Open-angle glaucoma because its involved in aqueous humor production [439]		
ADRs	Ocular irritation		
C.I	Asthma, COPD & heart block (especially non-selective); must be cautious with selective β ₁ .		

Treatment of Glaucoma

Open-angle (Chronic)

The main goal is to ↓ IOP by:

↓ Aqueous humor production

- β blockers
- α₂ agonists
- Carbonic anhydrase inhibitors

↑ Aqueous humor outflow

- Prostaglandins
- adrenergic agonists, nonspecific
- Parasympathomimetics

Prostaglandins & β blockers are the most popular.

	Carbonic Anhydrase Inhibitors		Prostaglandin Analogues	
Agent	Acetazolamide (oral)	Dorzolamide (topical)	Latanoprost (topical)	Travoprost (topical)
M.O.A.	<p>↓ Aqueous humor production by blocking carbonic anhydrase enzyme required for production of bicarbonate ions (transported to posterior chamber, carrying osmotic water flow).</p>		<p>↑ Uveoscleral aqueous outflow by vasodilation [439]. Latanoprost is preferred due to lesser ADRs & longer DOA → less frequency of administration</p>	
Uses	Open angle glaucoma			
ADRs	<p>Myopia, malaise, anorexia, GI upset, headache, mild metabolic acidosis & renal stones.</p>		<ul style="list-style-type: none"> ● Replaced β blockers. ● Used topically as eye drops & once a day. ● Pigmentation of iris (<i>heterochromia iridis</i>). The 2 eyes will have different colors ● Excessive hair growth of eye lashes 	
C.I	<ul style="list-style-type: none"> ● Sulpha allergy ● Pregnancy → decreases fetal weight (fetus is full of fluids) 		<p>-----</p>	

Treatment of Glaucoma

Narrow closed-angle (Acute)

Acute, painful increases of IOP due to occlusion of outflow drainage pathway. Thus, it is an **emergency** that requires treatment before surgery (**iridectomy**).

The use of drugs is limited to:

- Oral acetazolamide
- Topical cholinomimetics (e.g. Pilocarpine)
- Osmotic agents: hypertonic solutions of mannitol & glycerol.
- Analgesics for pain: Pethidine or Morphine.

Osmotic (Dehydrating) Agents

	Mannitol	Glycerol
M.O.A.	Rapidly lower IOP by decreasing vitreous volume prior to anterior surgical procedures.	
P.K.	IV infusion of hypertonic solution (mannitol, glycerol).	
	20% I.V.	50% syrup; oral
Uses	Used only in acute situations to temporarily reduce IOP until more definitive treatments can be given (short-term management).	
ADRs	<ul style="list-style-type: none"> • Diuresis, circulatory overload, pulmonary edema & heart failure. • CNS effects (e.g. seizures & cerebral hemorrhage). 	
	Fluid overload → not used in heart failure	Nausea, hyperglycemia & diarrhea
C.I	Heart failure	-----

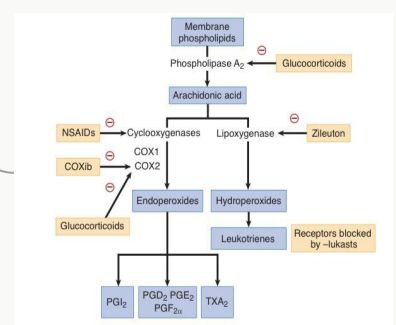
Anti-inflammatory Drugs

Important

Corticosteroids

memorize the examples

Drug	Systemic		Topical		
	Prednisolone	Cortisone	Prednisolone	Dexamethasone	Hydrocortisone
Uses	<ul style="list-style-type: none"> • Posterior uveitis • Optic neuritis 		<ul style="list-style-type: none"> • Anterior uveitis • Severe allergic conjunctivitis • Scleritis • Prevention & suppression of corneal graft rejection 		
M.O.A.	Inhibit arachidonic acid release from phospholipids by inhibiting phospholipase A₂				
Ocular ADRs	<ul style="list-style-type: none"> • Glaucoma, cataract & ↑ IOP & BP • Skin atrophy • Secondary infection due to immunosuppression • Delayed wound healing 				



NSAIDs

Drug	Flurbiprofen	Diclofenac (Voltaren)	Ketorolac
Uses	<p>Pre-operatively to prevent miosis during cataract surgery.</p> <p>When eye surgery causes trauma to the eye, inflammatory mediators are released, including PGs → miosis & hyperemia.</p>	<ul style="list-style-type: none"> ● Postoperatively ● Mild allergic conjunctivitis ● Mild uveitis 	<p>Cystoid macular edema that occurs after cataract surgery.</p> <p>Cystoid macular edema: a condition in which multi cyst-like areas in the macula are fluid-filled. In this case we can use NSAIDs or corticosteroids.</p>
M.O.A.	Inhibit cyclo-oxygenase (COX)		
ADRs	Stinging		

Drugs Causing Corneal Deposits

1	<p>Important</p> <p>Amiodarone (antiarrhythmic) & Chloroquine (antimalarial)</p>	<ul style="list-style-type: none"> ● Optic neuropathy with time ● Pigmented deposits of cornea
2	<p>Digitalis (cardiac failure drug)</p>	<p>Ocular disturbances & chromatopsia with overdose → objects appear yellow (<u>xanthopsia</u>).</p>
3	<p>Phenothiazines (antipsychotic & antiemetic)</p>	<p>Brown pigmentary deposits in the cornea, conjunctiva & eyelid</p>
4	<p>Steroids</p>	<ul style="list-style-type: none"> ● Cataract formation ● Elevated IOP & glaucoma
5	<p>Important</p> <p>Ethambutol (anti-TB)</p>	<ul style="list-style-type: none"> ● Optic neuropathy characterized by gradual progressive vision loss ● Red-green color blindness
6	<p>Sildenafil (Erectile Dysfunction)</p>	<ul style="list-style-type: none"> ● Bluish haze ● Light sensitivity

Summary

Indicator	Drugs	
Open-angle glaucoma	<ul style="list-style-type: none">• Non-selective agonists• Selective α_2 agonists• β Blockers	<ul style="list-style-type: none">• Direct & indirect cholinergic agonists• Prostaglandins• CA inhibitors
Closed-angle glaucoma	<ul style="list-style-type: none">• Oral Acetazolamide• Osmotic agents	<ul style="list-style-type: none">• Direct & indirect cholinergic agonists• Analgesics (for pain)
Fundoscopic examination of eye	<ul style="list-style-type: none">• Selective α_1 agonists• Non-selective agonists	<ul style="list-style-type: none">• Cholinergic antagonists
Prevention of adhesions in inflammation	<ul style="list-style-type: none">• Selective α_1 agonists• Non-selective agonists	<ul style="list-style-type: none">• Direct & indirect cholinergic agonists• Cholinergic antagonists



MCQ

1. what is the ANTI-TB medication that might cause optic neuropathy?

- | | | | |
|---------------|--------------|---------------|------------|
| A. Amiodarone | B. digitalis | C. Ethambutol | D. steroid |
|---------------|--------------|---------------|------------|

2. Which of the following drugs causes pigmented deposits of Cornea ?

- | | | | |
|-----------------|---------------|-------------|------------------|
| A. Flurbiprofen | B. Amiodarone | C. Mannitol | D. Apraclonidine |
|-----------------|---------------|-------------|------------------|

3. Which of the following drugs decrease aqueous humor production by blocking Carbonic Anhydrase enzyme ?

- | | | | |
|----------------|-------------|------------------|----------------|
| A. Latanoprost | B. Mannitol | C. Acetazolamide | D. Tropicamide |
|----------------|-------------|------------------|----------------|

4. Which of the following drugs is CONTRAINDICATED in Glaucoma ?

- | | | | |
|----------------|------------------|-------------|--------------|
| A. Latanoprost | B. Phenylephrine | C. Hyoscine | D. Betaxolol |
|----------------|------------------|-------------|--------------|

5. Which of the following drugs causes ocular disturbances and chromatopsia with overdose, resulting in the object appearing yellow ?

- | | | | |
|----------------|---------------|-------------------|--------------|
| A. Chloroquine | B. Sildenafil | C. Phenothiazines | D. Digitalis |
|----------------|---------------|-------------------|--------------|

6. is used before Cataract surgery to prevent miosis.

- | | | | |
|-----------------|-----------------|----------------|------------|
| A. Flurbiprofen | B. Prednisolone | C. Latanoprost | D. Timolol |
|-----------------|-----------------|----------------|------------|

7. Which of the following drugs causes myopia, malaise and mild metabolic acidosis?

- | | | | |
|---------------|-----------------|------------------|------------------|
| A. Travoprost | B. Prednisolone | C. Acetazolamide | D. Apraclonidine |
|---------------|-----------------|------------------|------------------|



SAQ

01

What drugs cause corneal deposits?

-Amiodarone, Chloroquine, Digitalis (yellow),
Phenothiazines (brown), Steroids, Ethambutol, Sildenafil
(blue)

02

What's the M.O.A. of Dexamethasone & ADRs?

ADRs: Glaucoma, cataract & \uparrow IOP, Skin atrophy,
Secondary infection, Delayed wound healing
M.O.A. Inhibit arachidonic acid release from
phospholipids by **inhibiting phospholipase A₂**

03

**Patient was diagnosis with open-angle glaucoma and he
has history with hypertension, which drug should we
describe for him?**

Beta blockers

Team Leaders

Muhannad Al-otabi

Reema Almotairi

Sarah Alajaji

Maryam Alghannam

Team members

Abdulaziz Alamri

Sami Mandoorah

Salma Alkhlassi

Faisal Alateeq

Omar Alamri



Huda bin jadaan

Nazmi M Alqutub

Mohammed Alqutub

Manar Aljanubi

Sultan Almishrafi

Reena Alsadoni

Wasan Alanazi

Mohammed Maashi

Almas Almutairi

Jana Almutlaqah

Mohammed Alasmary

Fatimah Alghamdi

Farah Abukhalaf

Nazmi A Alqutub

Lama Alotaibi

Norah Almalik

Ziad Alhabardi

Salma Alsaadoun

Rawan Alqahtani

Mohammed Alrobeia

Jouri Almaymoni

Aroub Almahmoud

Mohammed Alhudaithi



Faisal alzuhairy

Remaz Almahmoud

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