



## Ocular Pharmacology & Toxicology

[ **Color index:** **Important** | **Notes** | **Extra** ] [EDITING FILE](#)

### Objectives:

➤ Not given.

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**Resources:** Slides + 435 team F2(the original work was taken from it) + Notes

**Summary** [LINK](#)

(done by Reema Alnasser from last year)

**Key Points** [LINK](#)

(في حال قررتوا تسحبون عالمحاضرة مروا عليه اضعف الإيمان\*<sup>^</sup>)

# General Pharmacological Principles

## Pharmacodynamics:

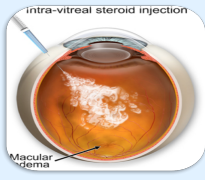
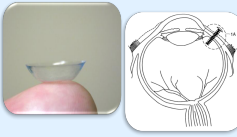
- **Mechanism of action:** it's the biological and therapeutic effect of the drug.
- Most drugs act by binding to regulatory macromolecule, usually neurotransmitters or enzymes or hormone receptors.
- If the drug is working at the **receptor level**, it can be **agonist or antagonist**.
- If the drug is working at the **enzyme level**, it can be **activator or inhibitor**.

## Pharmacodynamics:

It is the absorption, distribution, metabolism, and excretion of the drug : how the drug reach particular area and how it will be excreted. A drug can be delivered to ocular tissue as:

<p><b>1/ Eye Drops</b></p> <p>We prefer local on systemic b/c of more effect on target tissue and less side effects</p> 	<ul style="list-style-type: none"> <li>● <b>Most commonly used</b>, best way, can use it during day time.</li> <li>● one drop = 50 µl, <b>more than third of the drug will wash out, so 1 drop is more than enough.</b></li> <li>● volume of conjunctival cul-de-sac (the fornix of conjunctiva that act as reservoir of drug) <b>7-10 µl</b></li> <li>● <b>Measures to increase drop absorption, so increase effect:</b> (تنبهوا)             <ul style="list-style-type: none"> <li>○ Wait 5-10 minutes between drops</li> <li>○ Compress lacrimal sac, that will decrease systemic effect.</li> <li>○ Keep lids closed for 5 minutes after instillation (<b>blinking sucks the fluid from the ocular surface and drain it to the nasal cavity that's why we tell the patient to close his eyes</b>) increase local effect and decrease systemic effect</li> </ul> </li> </ul> <p>Once you open the bottle, if it preserved like in fridge you can use it till expiry date , if it outside the fridge then you can use for 1 month only</p>
<p><b>2/ Ointments</b></p> 	<ul style="list-style-type: none"> <li>● <b>Increase the contact time</b> of ocular medication to ocular surface thus better effect. <b>More viscous = stays for longer time</b></li> <li>● It has the disadvantage of <b>vision blurring</b> (Thick! advise pt to put it before going to sleep)</li> <li>● The drug has to be high lipid soluble with some water solubility to have the maximum effect as ointment.</li> </ul> <p><b>Note:</b> eye drops and ointments are more likely to affect anterior segment of the eye (cornea , conjunctiva, anterior chamber , the iris, lens and posterior chamber) but not any further, so if posterior segment of the eye is affected we need to use injection around the eye or directly to the eye.</p>
<p><b>3/ Peri-ocular injection</b></p> 	<ul style="list-style-type: none"> <li>● <b>Reach behind iris-lens diaphragm</b> better than topical application.</li> <li>● e.g. subconjunctival, subtenon (capsule surround the sclera and behind conjunctiva), peribulbar (around the globe → extraconal), or retrobulbar (behind the globe → intraconal)</li> <li>● This route bypass the conjunctival and corneal epithelium: <b>good for drugs with low lipid solubility</b> (e.g. penicillins).</li> <li>● Also steroid (reduce inflammation) and <b>local anesthetics*</b> can be applied this way</li> <li>● Use short needle or you will puncture the glop.</li> </ul> <p><b>*Notes about Local anesthesia for eye operation:</b></p> <p>1/ Topical eye drops → It numbs the surface (Anesthesia) but it doesn't block cranial nerves → the eye can move (no Akinesia) "this is good for cooperative patients". In uncooperative patients we need Anesthesia with Akinesia → retrobulbar or peribulbar block</p> <p>2/ Retrobulbar (Intraconal): depositing local anesthetic inside the muscle cone (which contains many vital structures: nerves / vessels and it is a confined area hemorrhage can increase the pressure in that area and damage these vital structures). It can lead to direct injury to the vital structures or retrobulbar hemorrhage (which can lead to central retinal artery occlusion and optic nerve atrophy. Emergent surgical intervention to decompress the orbit is needed)</p> <p>3/ Peribulbar (Extraconal) block: Safer and widely used compared to retrobulbar.</p>

Locally

<p><b>4/ Intraocular injections</b></p> 	<p>Intracameral(anterior chamber)or intravitreal delivers the medication directly into the eye.  <b>Examples:</b></p> <ul style="list-style-type: none"> <li>○ Intracameral acetylcholine (miochol) during cataract surgery. During cataract surgery, we put a lens inside the eye. How can we access the area behind the iris? We dilate the pupil → access the lens → aspirate it → put a lens. In order to secure the lens in position, we inject acetylcholine into the eye (parasympathomimetics) → constricts the pupil and lock the lens.</li> <li>○ Intravitreal antibiotics in cases of endophthalmitis a true ocular emergency that happens when an organism reaches the vitreous cavity and releases endotoxins that destroy the ocular tissue. Giving an antibiotic ASAP is essential.</li> <li>○ Intravitreal steroid in macular edema (diabetic patients)</li> <li>○ Intravitreal anti-VEGF(anti - vascular endothelial growth factor) for Diabetic retinopathy. the most recent method of treating diabetic retinopathy.</li> </ul>
<p><b>5/ Sustained-release devices</b></p> 	<p>These are devices that deliver an adequate supply of the medication at a steady-state level, These devices increase patients compliance by decreasing the frequency of administration.  <b>Examples:</b></p> <ol style="list-style-type: none"> <li>1. Ocusert delivering pilocarpine.</li> <li>2. Timoptic XE delivering timolol.</li> <li>3. Ganciclovir sustained-release intraocular device. Antiviral (CMV retinitis in cases of immunocompromised patients). We implant it surgically.</li> <li>4. Collagen shields. Dissolve in 2-3 hrs while the contact lens will not dissolve</li> </ol>
<p><b>Systemic</b></p>	<p>Oral or IV. (When do we use them? posterior segment or bilateral involvement of the eye / Autoimmune disease or TB Infection “the disease is outside the eye”/ or if there was a disease in the eye and I don’t want it to spread )  <b>Factor influencing systemic drug penetration into ocular tissue:</b></p> <ol style="list-style-type: none"> <li>1. <b>Lipid solubility of the drug:</b> more penetration with high lipid solubility , Major factor : more lipid binding less effect. Lipid solubility is favorable in case of systemic medications</li> <li>2. <b>Protein binding:</b> more effect with low protein binding. More protein binding = will not go to ocular tissue</li> <li>3. <b>Eye inflammation:</b> more penetration with ocular inflammation.so, when the eye is inflamed, we decrease the dose.</li> </ol>

## Factors influencing local drug penetration into ocular tissue EXAM

<p><b>1/ Drug concentration</b></p>	<p>The higher the concentration the better the penetration e.g. pilocarpine 1-4% but <u>limited by</u> reflex tearing.If you increase the concentration of a solution → more strong &amp; more <b>irritant</b> to the ocular tissue → release of tears. So they are testing different amounts of concentrations and they reach certain concentration beyond which the irritation will be less.</p>
<p><b>2/ Viscosity</b></p>	<p>Higher viscosity increases drug penetration by:</p> <ul style="list-style-type: none"> <li>● <u>Increasing the contact time with the cornea.</u></li> <li>● <u>Altering corneal epithelium.</u> More penetration to the ocular tissue.</li> </ul>
<p><b>3/ Lipid solubility</b></p>	<p><u>The higher lipid solubility the more the penetration</u> (because of the lipid rich environment of the epithelial cell membranes). (more lipophilic = more diffusion to the ocular tissue = more effect of the medication).</p>
<p><b>4/ Surfactants</b></p>	<p>The preservatives used in ocular preparations <u>alter cell membrane in the cornea</u> and increase drug permeability e.g. benzalkonium and thimerosal. Simply, surfactants are preservatives (compound added to medications to make these medications stable for certain period of time). There are some medications with or without preservatives. Preservatives alter (loosen) the junction between the cell membranes, so there will be more diffusion of the medication to the ocular tissue “damage to corneal epithelium”. Sometimes scraping of cornea is done to increase penetration “same idea”</p>

5/ pH	The normal tear pH is 7.4 (a little bit alkaline=alkaloid (شبه قلوي) and if the drug pH is much different, this will cause <b>reflex tearing</b> . Both acidic or alkaline are not desirable because both will be identified by the eye as irritants.
6/ Drug tonicity	When an alkaloid drug is put in relatively alkaloid medium, the proportion of the uncharged form will increase, thus more penetration. The non-ionized form of the medication is the active form. So if you want a non-ionized drug, you should make it more ALKALINE (~7.5, not so far from 7.4)

## Ocular Pharmacotherapeutics


Before starting you need to know the autonomic nervous system effect on the eye:

- Sympathetic NS → (1) pupil dilation “contraction of pupillary dilator or radial muscle” (2) decrease production of aqueous humor (3) retraction of the eye “contraction of muller muscle”
- Parasympathetic NS → (1) pupil constriction “contraction of pupillary constrictor or circular muscle” (2) increase production of aqueous humor. (3) Accommodation “contraction of ciliary muscle → suspensory ligament will relax → the lense will be rounded → optical power of the lense will increase “this help in near object vision, it will bring the image on the retina”

Accommodation is accompanied by 2 things: 1) convergence. 2) miosis. All these brings the image on the retina. As lense accommodation increase the refractive power, the convergence of the eyes will keep the image in the center of fovea, and miosis increase the depth of focus of the eye by blocking the light scattered by the periphery of the cornea. [See the video here.](#)

**Note: anti-glaucoma medication. Patient takes it for life.**

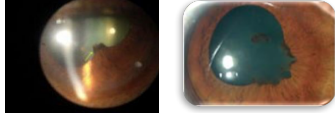
## Cholinergic agonist

<b>Directly acting agonists:</b>	<b>Indirectly acting (anticholinesterases):</b> More potent with longer duration of action (act by binding to cholinesterase, the inhibition of this enzyme could be reversible or irreversible)	
[pilocarpine, acetylcholine (miochol), carbachol (miostat)]	<b>Reversible inhibitors</b> [Physostigmine used in Myasthenia Gravis]. Less potent, not commonly used	<b>Irreversible inhibitors</b> [e.g.phospholine iodide].
To Induce miosis, for glaucoma.	<b>uses:</b> <ul style="list-style-type: none"> <li>• glaucoma</li> </ul> <p>We use it to treat glaucoma as it increase the aqueous outflow (drainage to the circulation = less fluid in the eye = less pressure).</p> <ul style="list-style-type: none"> <li>• lice infestation of lashes. يسبب نيوروتوكسينتي للقمل ويموتون</li> </ul>	<ul style="list-style-type: none"> <li>• Used in <b>accommodative esotropia</b>. </li> <li>- Esotropia = Eyes in</li> <li>- Exotropia = Eyes out</li> <li>These children are usually hyperopia which means that the image is formed behind the retina. Accommodation increases the refractive power of the eye and brings the image from behind the retina to the retina.</li> <li>- When someone accommodates or changes his refractive power 2 things happen: 1) miosis 2) conversion. (eyes will go in). So, when these children try to accommodate, the 2 things (miosis &amp; conversion) happen. This explains why they have esotropia.</li> <li>- <b>We use this medication to induce accomodation without actively having the child to accommodate himself.</b> (they have strabismus when focusing in typically farsightedness)</li> </ul>
<b>Mechanism of action:</b> <ul style="list-style-type: none"> <li>• Miosis by contraction of the iris sphincter muscle.</li> <li>• Accommodation by <u>circular</u> ciliary muscle contraction. A change in lens refractive power in order to see the nearer objects.</li> <li>• <b>Increases aqueous outflow</b> (inside eye to outside) through the trabecular meshwork by <u>longitudinal</u> ciliary muscle contraction. Contraction of the longitudinal ciliary muscle &gt; <b>the spaces in trabecular meshwork will open</b> &gt; more fluid will go to the circulation.</li> <li>• Note that in people with hyperopia “the eye is small” this mechanism can lead to iridolenticular apposition → glaucoma</li> </ul>		

<p><b>Side effects:</b>  <b>Local:</b> diminished vision (<b>myopia</b> with long use. Why? 1. Optical power is increased and 2. the contraction of longitudinal ciliary muscle will bring the lense forward → focal point will be in front of retina), <b>headache</b> (continuous contraction of the ciliary muscle), cataract, miotic cysts, and rarely retinal detachment.  <b>Systemic:</b> diarrhea, lacrimation, salivation, perspiration, bronchospasm, nausea, vomiting and urinary urgency.</p>	<p><b>Side effect:</b>  <b>CNS</b> side effects.</p>	<p><b>Side effect:</b>  Iris cyst  Anterior subcapsular cataract  <b>Can causes apnea if used with succinylcholine or procaine. Use atracurium as an alternative.</b>  <b>Contraindications (special):</b>  angle <b>closure</b> glaucoma</p>
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**Contraindications:** asthma, Parkinsonism

## Cholinergic antagonist

Cholinergic antagonists	
<b>Examples</b>	Tropicamide (6 hrs), cyclopentolate, homatropine, <b>atropine (10-14 DAYS)</b>
<b>Cause</b>	Mydriasis (by paralyzing the sphincter muscle) with cycloplegia (by paralyzing the ciliary muscle (so there will be loss of accommodation, warn the patient that they won't be able to read for a few hours (اضروري يمكن يكون عنده شغله تحتاج تركيز))
<b>Uses</b>	<p>Fundoscopy, cycloplegic refraction (procedure to <u>measure the refractive error</u> by temporarily paralyzing the muscles that aid in the accommodation because if there is <b>acomodation</b> the result would be wrong glass prescription. Thus, measurement will be precise.), <b>anterior uveitis</b> (inflammation → adhesion. We give it to decrease the contact between the iris and the lens → decrease adhesions), Cycloplegic drop help manage pain when there is inflammation in the eye, the ciliary body may spasm, causing pain.</p> <div style="display: flex; justify-content: center; align-items: center;">  <div style="margin-left: 10px;"> <p><b>Pic: Adhesion of the iris to the lense AKA posterior synechiae</b></p> </div> </div>
<b>Side effects</b>	<ul style="list-style-type: none"> <li>● <b>local:</b> <b>allergic reaction</b>, blurred vision <b>especially in bright light</b></li> <li>● <b>Systemic:</b> nausea, vomiting, pallor, vasomotor collapse, constipation, urinary retention, and confusion <ul style="list-style-type: none"> <li>→ Specially <b>in children</b> they might cause flushing, fever, tachycardia, or delirium</li> <li>→ Treatment by DC (direct cholinergic) or physostigmine <b>as an antidote</b></li> </ul> </li> </ul>



# Adrenergic agonists

Non-selective agonists	Selective agonists	
<p>(<math>\alpha_1</math>, <math>\alpha_2</math>, <math>\beta_1</math>, <math>\beta_2</math>) E.g. epinephrine, dipivefrin (prodrug of epinephrine)</p>	<p><b>Alpha-1 agonists</b> (e.g. phenylephrine) <b>work on muscle</b></p>	<p><b>Alpha-2 agonists</b> (e.g. brimonidine, apraclonidine) <b>decreases the pressure</b></p>
<p>Used in glaucoma <b>in the past</b></p>	<ul style="list-style-type: none"> <li>• <b>Used to induce Mydriasis (without cycloplegia)</b> for fundus evaluation, they do not have effect on the ciliary muscle,   → Q)WHAT IS THE MEDICATION THAT CAUSES MYDRIASIS WITHOUT CYCLOPLEGIA? يجيبك سؤال وحده عندها اختبار بعد العيادة وانتي تبين تسوينلها فوندىس اقزامنيشن وش افضل قطرات تحطينا بحيث ماتأثر عالقراءه</li> <li>• <b>decongestant it is a vasoconstrictor</b></li> </ul>	<ul style="list-style-type: none"> <li>• <b>Uses:</b> glaucoma treatment [treatment of the <b>open</b> angle not the closure angle] and prophylaxis after glaucoma laser procedures.</li> <li>• <b>Mechanism:</b> <b>decrease aqueous production, and increase uveoscleral drainage</b> (drainage 90% by canal of schlemm, 10% outflow uveoscleral) <b>most of the drainage happen through trabecular meshwork (conventional). This medication affects only the uveoscleral one.</b></li> </ul>
<p><b>Side effects:</b></p> <ul style="list-style-type: none"> <li>• Headache, arrhythmia, <b>increased blood pressure,</b></li> <li>• <b>cystoid macular edema in aphakic eyes.</b>  phakic=lens, pseudophakic= artificial lens, Aphakic=no lense زمان لما كانوا يشيلوا الكتر اکت ماكانوا يحطون عدسات مكانها ماكانوا مكتشفين انه ممكن تتركب العدسه داخل العين , طيب فلو هذول الاشخاص استخدموا ابنيفرن مرح يصير فيه حاجز على طول بتدخل القطره للريتينا و الماكيو لا مكونه سيست</li> <li>• <b>conjunctival adrenochrome</b> (pigments/black dots in conjunctival fornix in pt use adrenergic drugs <b>chronic users of epinephrine</b>)”pic”</li> </ul> <p>Pic : notice the small dots if present, you have to ask about these drug, the dots are dangerous because it is a pigmentation lesion.</p> 	<p><b>Side effect:</b></p> <ul style="list-style-type: none"> <li>• Can cause significant <b>increase blood pressure</b> especially in infant and susceptible adults</li> <li>• Rebound congestion</li> <li>• Induce acute angle-closure glaucoma in patients with narrow angles</li> </ul>	<p><b>Side effect:</b></p> <ul style="list-style-type: none"> <li>• <b>Local:</b> allergic reaction, mydriasis, Conjunctival blanching (pale), <b>lid retraction</b> (it activates sympathetic which innervates muller muscle).</li> </ul> <p><b>In the exam: pic &amp; asking which eye is using <math>\alpha_2</math> agonist? The more opened eye.</b></p> <ul style="list-style-type: none"> <li>• <b>Systemic:</b> oral dryness, headache, fatigue, drowsiness, orthostatic hypotension, vasovagal attacks</li> </ul>
<p><b>Contraindications:</b></p> <ul style="list-style-type: none"> <li>• <b>closed</b> angle glaucoma <b>can cause crowding of the angle</b></li> <li>• cardiac patient.</li> </ul>	<p><b>Contraindications:</b></p> <ul style="list-style-type: none"> <li>• infants <b>because of their CNS side effects</b></li> <li>• MAO inhibitors users <b>tendency to increase BP</b>  *MAO: monoamine oxidase inhibitors for depression</li> </ul>	

★ فإذا عمرنا مانستخدم adrenergic agonist مع ال **closed** angle glaucoma !! لأنها تصغر الزاويه اكثر فتزيد الأمور سواةا!!!! it dilates the pupil and draws the peripheral iris toward the angle!!!!  
اتقنا لاتسونها طول حياتكم ٨.٨

## Adrenergic antagonists

Alpha adrenergic antagonists	Beta-adrenergic antagonists (the most effective initial treatment of open glaucoma)
E.g. thymoxamine, dapiprazole	<ul style="list-style-type: none"> <li>● <b>Nonselective:</b> timolol, levobunolol, metipranolol, carteolol</li> <li>● <b>Selective:</b> betaxolol (beta 1 “cardioselective”) (Good for asthmatic)</li> </ul>
<b>Uses:</b> to reverse pupil dilation produced by phenylephrine (better not to be used because of the risk of retinal detachment) <b>Not widely used</b>	<ul style="list-style-type: none"> <li>● <b>Uses:</b> glaucoma (commonly used to treat glaucoma because of their action on reducing the formation of aqueous by ciliary body)</li> <li>● <b>Mechanism:</b> reduce the formation of aqueous humor by the ciliary body.</li> </ul>
	<b>Side effects:</b> <b>bronchospasm</b> (less with betaxolol) (non-selective: exacerbates bronchial asthma, COPD ), cardiac impairment

## Carbonic anhydrase inhibitors

<b>Examples</b>	<b>Acetazolamide</b> , methazolamide, dichlorphenamide, dorzolamide, brinzolamide.
<b>Mechanism</b>	<b>aqueous suppression</b> (carbonic anhydrase have a role in producing aqueous humor)
<b>Uses</b>	glaucoma (if not respond to other meds), cystoid <b>macular edema</b> (previous mcqs), <b>pseudotumor cerebri (= idiopathic intracranial hypertension)</b> Increased ICP without the presence of a tumor, we use it to decrease production of CSF. CSF → ↑ ICP → resembling tumor لوحظ انه يحصل بالنساء السمينات يقل عندهم الدرينج ل
<b>Side effects</b>	myopia, <b>paresthesia</b> circumoral numbness and <b>peripheral numbness</b> , anorexia, GI upset, headache, altered taste and smell, Na and K depletion, metabolic acidosis <b>normal anion gap</b> , <b>renal stone</b> , bone marrow suppression “ <i>aplastic anemia</i> ”.
<b>Contraindications</b>	sulfa allergy it's sulfa derivative, digitalis users <b>lethal hypokalemia</b> , pregnancy

## Osmotic agents

**(Used to suppress IOP as fast as possible in Acute attacks):** Dehydrate vitreous body which reduce IOP **significantly** loading the circulation with high concentration of fluid > less conc. In the vitreous > the water will go from lesser to higher concentration, we are basically dehydrating the vitreous.

**Examples are:**

1. Glycerol 50% syrup (cause nausea, hyperglycemia) **oral, caution in uncontrolled DM**
2. Mannitol 20% IV (**cause fluid overload, avoid in heart failure and renal impairment!!!**) (evaluate CVS before use)

Use in case of acute angle closure glaucoma to reduce IOP rapidly.

## Prostaglandin analogue

★ **CASE:** patient has bronchial **asthma** and **high blood pressure** presented with open angle glaucoma. the most appropriate drug to treat glaucoma? Prostaglandins Analogue

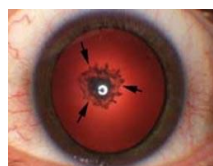
- E.g. latanoprost, bimatoprost, travoprost, unoprostone.
- **Uses:** glaucoma.
- **Mechanism:** increase **uveoscleral** aqueous outflow.



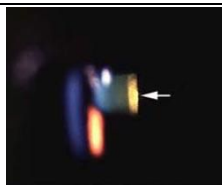
**Side effects:** darkening of the iris (**heterochromia iridis**) الصورة جت بملك سابق, lengthening and thickening of eyelashes عطني واحد بروستاغلاندين بليز; p, intraocular inflammation because it's an inflammatory mediator, macular edema.

# Anti-inflammatory it's very important to know the side effect of corticosteroid

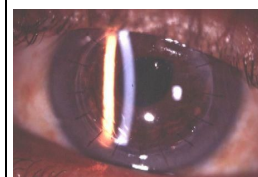
Corticosteroids			NSAIDS
	Topical	Systemic	
<b>Example</b>	<ul style="list-style-type: none"> <li>Fluorometholone</li> <li>Remixolone</li> <li>Prednisolone</li> <li>Dexamethasone</li> <li>hydrocortisone</li> </ul>	<ul style="list-style-type: none"> <li>Prednisolone</li> <li>cortisone</li> </ul>	<ul style="list-style-type: none"> <li>Ketorolac,</li> <li>Diclofenac</li> <li>flurbiprofen</li> </ul>
<b>uses</b>	<ul style="list-style-type: none"> <li>Postoperatively</li> <li>Anterior uveitis</li> <li><u>Severe</u> allergic conjunctivitis <small>we don't use it as 1st line, only if other medications failed.</small></li> <li>Vernal keratoconjunctivitis (<u>severe</u> form of ocular allergy)</li> <li>Prevention and suppression of corneal graft rejection</li> <li>Episcleritis</li> <li>Scleritis</li> </ul>	<ul style="list-style-type: none"> <li>Posterior uveitis</li> <li>Optic neuritis</li> <li>Temporal arteritis with anterior ischemic optic neuropathy.</li> </ul>	<ul style="list-style-type: none"> <li>Postoperatively</li> <li><u>Mild</u> allergic conjunctivitis</li> <li>Episcleritis</li> <li><u>Mild</u> uveitis</li> <li>Cystoid macular edema</li> <li>Preoperatively to prevent miosis during surgery "to inhibit prostaglandin which is known to constrict the pupil"</li> </ul>
<b>Mechanism</b>	inhibition of arachidonic acid release from phospholipids by <b>inhibiting phospholipase A2 (very potent)</b>		<b>Inactivation of cyclooxygenase enzyme</b> (prevent formation of PG which causes miosis, so we use it in cataract surgery)
<b>Side Effects</b>	<ul style="list-style-type: none"> <li><b>Susceptibility to infections</b></li> <li><b>Glaucoma</b></li> <li><b>Cataract</b></li> <li>Ptosis</li> <li>Mydriasis</li> <li>Scleral melting</li> <li>Skin atrophy</li> </ul> <p>على كثر البلاوي الي تسويها بالعين بس انتبهوا انها ماتسبب اوبتك نيور ايتس فلايلخيطونكم بالخيارات (:</p> <ul style="list-style-type: none"> <li><b>The most serious side effect of topical steroids is increased IOP (STEROID INDUCED GLAUCOMA) asymptomatic, permanent damage.</b></li> </ul>	<p><b>Local:</b> <b>posterior subcapsular cataract</b>, glaucoma, central serous retinopathy</p> <p><b>Systemic:</b> suppression of pituitary-adrenal axis, hyperglycemia, osteoporosis, peptic ulcer, psychosis</p>	<ul style="list-style-type: none"> <li>Stinging.</li> </ul>



Posterior subcapsular cataract "retroillumination"



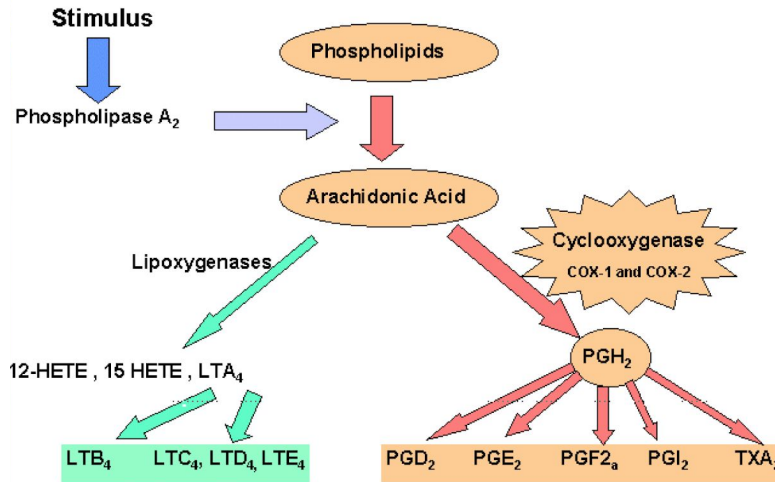
Posterior subcapsular cataract "slit lamp"



Posterior subcapsular cataract "slit lamp"



Figure 2 : Biosynthesis of eicosanoids



## Anti Allergic

★ **Remember:** the use of antiAllergic should be (**temporary**): antihistamine or steroids (only prescribed in serious situations and for a short period because of the serious side effects).

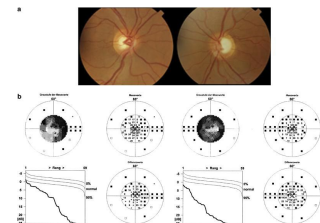
Type	Example	Mechanism and Uses	Side Effect
<b>Antihistamines</b>	Pheniramine levocabastine	Work by <b>blocking histamine</b> that is produced by the body in response to allergens or irritants	Drowsiness. bradycardia and overdose may lead to sleep disorders.
<b>Decongestants</b>	naphazoline phenylephrine tetrahydrozoline	used to relieve redness, puffiness, and itchy/watering eyes due to colds, allergies, or eye irritations	Stinging. Redness. widened pupils, or blurred vision.
<b>Mast cell stabilizers</b>	cromolyn, lodoxamide pemirolast nedocromil olopatadine	They <b>block a calcium channel</b> essential for mast cell degranulation, stabilizing the cell and thereby <b>preventing the release of histamine</b> and related mediators.	-
<b>NSAID</b>	Ketorolac	-	Stevens Johnson syndrome.
<b>Corticosteroids</b>	Fluorometholone remixolone prednisolone	-	Posterior subcapsular cataract. Glaucoma. Papilledema. Predisposition to fungal infections. لو جاكم سؤال وحده عندها الرجى بالكونجكتافا وطاحت على دواء يخففها وصارت كل شوي كل شوي تستخدمه لين صار لها high IOP ايش هو الدواء ياترى : ( ماغيره كورتيكوستيرويد

### Tips:

- ✓ Avoidance of allergens, cold compress (استخدم تلج عشان نسوي كونستر كشن للفيزيوليس فماعاد يوصل دم ولا انفلاماتوري سيلز للمنطقه ونفتك منها ومن غتاها), lubrications.
- ✓ Drug combinations (if needed)



Chemosis : (روحوا ابحتوا وش تعني يورهوم وورك):



cupping "visual field defect" seen in advanced glaucoma

## EXTRA PAGE Taken from Lecture Note book:

لأمانه ترتيب السلايدز (الترتيب السابق) لأدويه الجلوكوما موعاجبني ابد : هذا ترتيب ثاني حسب نوع الجلوكوما

### Chronic Open angle glaucoma

#### Medical treatment:

In chronic open angle glaucoma the **prostaglandin analogues** are becoming the first-line treatment. They act by increasing the passage of aqueous through the uveoscleral pathway. Topical adrenergic **beta-blockers** may further reduce the pressure by suppressing aqueous secretion. Non-selective beta-blockers carry the risk of precipitating asthma through their beta-2 blocking action, following systemic absorption, or they may exacerbate an existing heart block through their beta-1 action. **Pilocarpine** may occasionally be used in the treatment of chronic open angle glaucoma.

If intraocular pressure remains elevated the choice lies between:

- **adding additional medical treatment**
- **laser treatment**
- **surgical drainage procedures**

### Primary angle Closure glaucoma

The acute and dramatic rise in pressure seen in angle closure glaucoma must be **urgently** countered to prevent permanent damage to the vision.

- **Medical treatment(initially): Acetazolamide** is administered intravenously and subsequently orally, together with topical **pilocarpine** and **beta-blockers**. Pilocarpine constricts the pupil and draws the peripheral iris out of the angle; the acetazolamide and beta-blocker reduce aqueous secretion and the pressure gradient across the iris. These measures often break the attack and lower intraocular pressure.
- **Subsequent management requires that a small hole (iridotomy or iridectomy) be made in the peripheral iris to prevent further attacks.** This provides an alternative pathway for fluid to flow from the posterior to the anterior chamber, bypassing the pupil and thus reducing the pressure gradient across the iris. This can be done with a YAG laser or surgically.

### Congenital glaucoma

#### Congenital glaucoma is usually treated **surgically**:

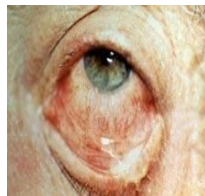
An incision is made into the trabecular meshwork (goniotomy) to increase aqueous drainage, or a direct passage between Schlemm's canal and the anterior chamber is created (trabeculotomy).

### Secondary glaucoma

Treatment broadly follows the lines of the primary disease. In secondary glaucoma it is important to treat any underlying cause, e.g. uveitis, which may be responsible for the glaucoma

# Antibiotics

<b>Examples</b>	Penicillins, Tetracyclines, Fluoroquinolones, Cephalosporins, Chloramphenicol, Vancomycin Sulfonamides, Aminoglycosides, Macrolides.
<b>Uses</b> موضع أسنله لاتسلكون لها تراها اعاده لدرس الاكويولر امير جنسي	<ul style="list-style-type: none"> <li>Used <b>topically</b> in prophylaxis (pre and postoperatively) and treatment of ocular bacterial infections.</li> <li>Used <b>orally</b> for the treatment of preseptal cellulitis e.g. amoxicillin with clavulanate, cefaclor. <i>If there is an inflammation or infection in front of orbital septum &gt; preseptal cellulitis &gt; we use oral antibiotics. If the inflammation or infection is behind this septum &gt; orbital cellulitis &gt; a true ophthalmic emergency that can progress to meningitis or encephalitis or cavernous sinus thrombosis or periosteal abscess, that's why we treat it aggressively with <b>IV</b> antibiotics + admit the patient.</i></li> <li>Used <b>intravenously</b> for the treatment of orbital cellulitis e.g. gentamicin, cephalosporin, vancomycin, flagyl.</li> <li>Can be injected <b>intravitreally</b> for the treatment of <b>endophthalmitis</b>. <i>a true ophthalmic emergency that has to be treated by injecting the antibiotic directly to the eye, otherwise nothing can help! Hypopyon (collection of pus in the anterior chamber) is a sign of endophthalmitis.</i></li> <li><b>Trachoma</b> can be treated by topical <b>and</b> systemic tetracycline or erythromycin, or systemic azithromycin. <i>Caused by chlamydia trachomatis</i></li> <li><b>Bacterial keratitis</b> (bacterial corneal ulcers) can be treated by <u>topical fortified</u> penicillins, cephalosporins, aminoglycosides, vancomycin, or fluoroquinolones <b>"hourly"</b>. <i>Keratitis = cornea, there will be opacity. It can affect the vision permanently. Treat it with TOPICAL Abx EVERY HOUR even if the pt is sleeping.</i></li> <li><b>Bacterial conjunctivitis</b> is usually self-limited but topical erythromycin, aminoglycosides, fluoroquinolones, or chloramphenicol can be used. <i>Broad spectrum Abx</i></li> </ul>



Ectropion



Endophthalmitis



Corneal Ulcer

# Antifungal

**Uses:** fungal keratitis, fungal endophthalmitis.

**1/ Polyenes:** E.g. amphotericin B, natamycin.

Damage cell membrane of susceptible fungi.

Side effect: nephrotoxicity.

**2/ Imidazoles:** E.g. miconazole, ketoconazole.

Increase fungal cell membrane permeability.

**3/ Flucytosine:**

Act by inhibiting DNA synthesis

# Antiviral

<b>Acyclovir</b>	<ul style="list-style-type: none"> <li>interact with viral thymidine.</li> <li>Kinase (selective).</li> <li>Used in herpetic keratitis.</li> </ul> <p><b>This picture could come in the exam &gt; Stained eye showing dendritic shape ulcer &gt; herpetic keratitis in fluorescein stain .</b></p>	
<b>Trifluridine</b>	<ul style="list-style-type: none"> <li><b>More</b> corneal penetration.</li> <li>Can treat herpetic iritis.</li> </ul>	
<b>Ganciclovir</b>	<ul style="list-style-type: none"> <li>Used intravenously for <b>CMV Retinitis</b>. <i>Immunocompromised pts.</i></li> </ul>	

# Ocular diagnostic drugs

ادري انكم بديتوا تطفون لما وصلتوا هالنقطة بس ركزوا بكل حرف فيها جزئيه سهله مره بس يحدوون يسألون عنها):

## Fluorescein dye:

it goes to the area that doesn't have epithelium, so if the surface epithelium is deficient in some area, it will be stained by Fluorescein. Available as drops or strips

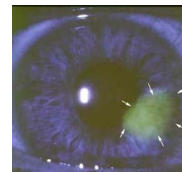
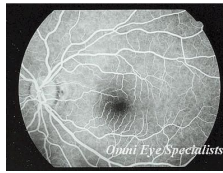
**Uses:** stain corneal abrasions, applanation tonometry to measure IOP, detecting wound leak, nasolacrimal duct obstruction If a patient came to you with tearing in the right eye, but the Fluorescein in the eye and check it after 5 minutes, after that, if you find more Fluorescein in the eye it means that the Fluorescein did not go to the nasal cavity means that there is some blockage in the nasolacrimal duct. That's how we diagnose NLD obstruction., fluorescein angiography I.V. > retinal circulation.

### Caution!

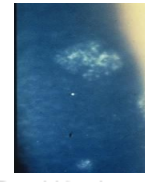
- ★ Stains soft contact lens. so before staining Ask if the patient is wearing any contact lens as fluorescein might stain it permanently
- ★ Fluorescein drops can be contaminated by Pseudomonas sp.

### Normal Fluorescein angiography

In the normal macula, the capillary-free zone is seen as dark due to blockage of choroidal fluorescence retinal pigment epithelial cells



Abrasion stain

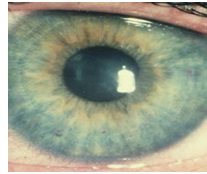


Dendritic ulcer staining with fluorescein

## Rose Bengal Stain:

Stains devitalized epithelium.

**Uses:** severe dry eye (use it if u suspect sjogren's syndrome), herpetic keratitis



## Local anesthesia

### 1/ Topical: E.g. proparacaine, tetracaine.

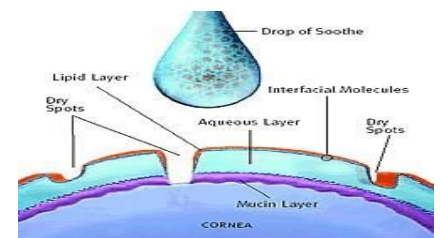
- **Uses:** applanation tonometry, gonioscopy viewing the angle of the eye, removal of corneal foreign bodies, removal of sutures, examination of patients who cannot open eyes because of pain.
- **Adverse effects:** toxic to corneal epithelium, allergic reaction rarely.

### 2/ Orbital infiltration: Peribulbar or retrobulbar.

- Cause anesthesia and akinesia for intraocular surgery. E.g. lidocaine, bupivacaine.

## Lubricants

- Drops or ointments.
- Polyvinyl alcohol, cellulose, methylcellulose.
- Preserved or preservative free. **Less irritation**


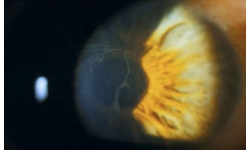

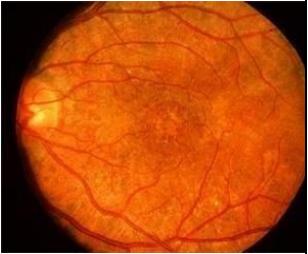


# Ocular toxicology


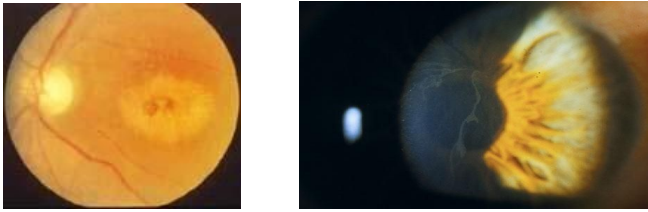
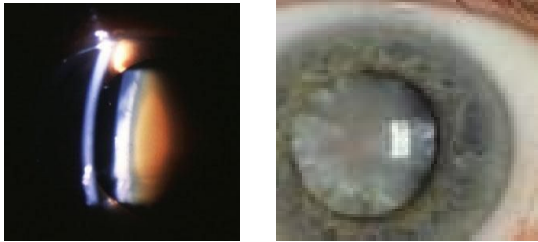
## Complications of topical administration

- Mechanical injury from the bottle e.g. corneal abrasion.
- Pigmentation: epinephrine adrenochrome.
- Ocular damage: e.g. topical anesthetics, benzalkonium.
- Hypersensitivity: e.g. atropine, neomycin, gentamicin.
- Systemic effect: topical phenylephrine can increase BP.

## Drugs associated with ocular toxicity

Drug	Effect
<b>Amiodarone</b>	<ul style="list-style-type: none"> <li>• A cardiac arrhythmia drug.</li> <li>• <b>Causes optic neuropathy</b> (mild decreased vision, visual field defects, bilateral optic disc swelling)                              </li> <li>• Also causes <b>corneal vortex keratopathy (corneal verticillata)</b> which is whorl-shaped pigmented deposits in the corneal epithelium.                              </li> </ul>
<b>Digitalis</b>	<ul style="list-style-type: none"> <li>• A cardiac failure drug.</li> <li>• Causes <b>chromatopsia (objects appear yellow)</b> with overdose. <b>abnormal perception of color.</b> If the object appears yellow &gt; xanthopsia. (اموت اذا ماسألوا عنها.)</li> </ul> 
<b>Chlorpromazine</b>	<ul style="list-style-type: none"> <li>• A psychiatric drug</li> <li>• Causes corneal punctate epithelial opacities, lens surface opacities</li> <li>• Rarely symptomatic</li> <li>• Reversible with drug discontinuation.</li> </ul>
<b>Thioridazine</b>	<ul style="list-style-type: none"> <li>• A psychiatric drug</li> <li>• Causes a pigmentary retinopathy after <u>high dosage</u></li> <li>• <b><u>SALT AND PEPPER APPEARANCE</u></b></li> </ul> 



<p><b>Diphenylhydantoin</b></p>	<ul style="list-style-type: none"> <li>● An epilepsy drug</li> <li>● Causes dosage-related cerebellar-vestibular effects: <ul style="list-style-type: none"> <li>○ Horizontal <b>nystagmus</b> in lateral gaze</li> <li>○ <b>Diplopia, ophthalmoplegia</b></li> <li>○ Vertigo, ataxia</li> </ul> </li> <li>● Reversible with the discontinuation of the drug</li> </ul>
<p><b>Topiramate</b></p>	<ul style="list-style-type: none"> <li>● A drug for epilepsy</li> <li>● Causes <b>acute angle-closure glaucoma</b> (acute eye pain, redness, blurred vision, halos).</li> <li>● Treatment of this type of acute angle-closure glaucoma is by cycloplegia and topical steroids (rather than iridectomy) with the discontinuation of the drug</li> </ul>
<p><b>Ethambutol</b></p>	<ul style="list-style-type: none"> <li>● An anti-TB drug</li> <li>● Causes a <b>dose-related optic neuropathy</b></li> <li>● Usually reversible but occasionally permanent visual damage might occur</li> </ul> 
<p><b>Chloroquine</b></p>	<ul style="list-style-type: none"> <li>● E.g. chloroquine, hydroxychloroquine</li> <li>● Used in malaria, rheumatoid arthritis, SLE</li> <li>● Cause vortex keratopathy (corneal verticillata) which is usually asymptomatic but can present with glare and photophobia</li> <li>● Also cause retinopathy (<b>bull's eye maculopathy</b>)</li> <li>● <b>vortex keratopathy could be caused by BOTH amiodarone and Chloroquine.</b></li> </ul> 
<p><b>HMG-CoA REDUCTASE INHIBITORS (STATINS):</b></p>	<ul style="list-style-type: none"> <li>● E.g. pravastatin, lovastatin, simvastatin, fluvastatin, atorvastatin, rosuvastatin</li> <li>● Cholesterol lowering agents.</li> <li>● <b>Can cause cataract in high doses especially if used with erythromycin</b></li> </ul> 
<p><b>Methanol</b></p>	<p>Optic atrophy and blindness (Patient presents with history of alcohol drinking).</p>
<p><b>Contraceptive pills</b></p>	<p>Pseudotumor cerebri (papilledema), and dryness (CL intolerance)</p>
<p><b>Chloramphenicol and streptomycin</b></p>	<p>Optic atrophy</p>
<p><b>Hypervitaminosis A</b></p>	<p>Yellow skin and conjunctiva, pseudotumor cerebri (papilledema), retinal hemorrhage.</p>
<p><b>Hypovitaminosis A</b></p>	<p>Night blindness (nyctalopia), keratomalacia.</p>

## Agents that can cause Toxic Optic Neuropathy

- **Methanol (IMP!!!)** Can cause bilateral blindness
- Ethylene glycol (antifreeze)
- **Chloramphenicol**
- **Isoniazid**
- Carbon monoxide
- **Lead**
- **Mercury**
- **Ethambutol**
- **Digitalis**
- Chloroquine
- **Streptomycin**
- Thallium (alopecia, skin rash, severe vision loss)
- Malnutrition with vitamin B-1 deficiency
- **Amiodarone**
- Quinine
- Methotrexate
- Pernicious anemia (vitamin B12 malabsorption phenomenon)
- Vincristine and methotrexate (chemotherapy medicines)
- Sulfonamides
- Melatonin with Zoloft (sertraline, Pfizer) in a high-protein diet
- Radiation unshielded (exposure to >3,000 rads).