

Ocular Pharmacology -II

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Learning Objectives

At the end of this class students shall have a basic understanding of :

- Therapeutic agents for glaucoma
- Anti-inflammatory agents
- Tear substitutes
- Drugs and biological agents used in Ophthalmic surgery
- Ocular toxicology

Overview

Overview of ocular anatomy & physiology

Pharmacodynamics and Pharmacokinetics of ocular therapeutic agents

Ocular Routes of Drug Administration

Therapeutic & Diagnostic applications of Drugs in Ophthalmology

Ophthalmic Effects of Selected Vitamin Deficiencies

Systemic Agents with Ocular Side Effects

Conclusion

Agents used for treatment of Open angle Glaucoma

1. Prostaglandin analogues
2. Beta receptor antagonists
3. Alpha receptor agonists
4. Carbonic anhydrase inhibitors

Prostaglandin Analogs

First- line medical therapy for Glaucoma

PGF₂ α analogs -

Good efficacy

Once daily application

Absence of systemic side effects

1.Latanoprost 2. Travoprost 3.Bimatoprost

Facilitate aqueous outflow through uveoscleral outflow pathway

Prostaglandin Analogs

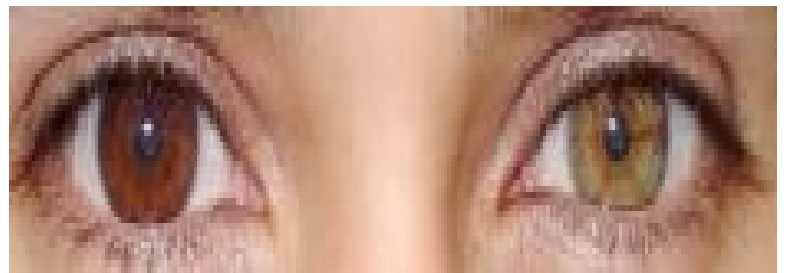
Side effects

Ocular irritation & pain

Blurring of vision

Increased iris pigmentation

Macular edema



β Adrenergic blockers

- Nonselective β blockers – Timolol maleate
 - Levobunolol
 - Metipranolol
 - Carteolol

- β -1 antagonist
 - Betaxolol

Mechanism of Action of β Blockers

- Lower IOP by reducing aqueous formation
 - Down regulation of adenylylcyclase due to β 2 receptor blockade in ciliary epithelium
 - Reduction in ocular blood flow

Adverse Effects of Ocular β Adrenergic blockers

Ocular

1. Stinging, redness & dryness of eye
2. Corneal hypoesthesia
3. Allergic blepharoconjunctivitis
4. Blurred vision

Systemic

1. Bronchospasm in asthmatics & COPD patients
2. Bradycardia & accentuation of Heart block

Minimization of systemic adverse effects

Alpha Adrenergic agonists

- Brimonidine (Alpha-2 agonist)(0.1%,0.2%)
- Usually used as an add on agent
- Mainly reduces aqueous production
- Also increases uveoscleral outflow
- To be used cautiously in children and elderly as it may cause **fatigue and drowsiness**.

Carbonic anhydrase Inhibitors (CAI)

- Systemic -Acetazolamide
- Topical CAI – Dorzolamide , Brinzolamide
- Inhibits carbonic anhydrase (isoenzyme II) on ciliary body epithelium → Reduces formation of bicarbonate ions → Reduces fluid transport → Reduces aqueous formation → Decrease IOP
- Use – Only as add on drug to topical β blockers or PG analogs

Systemic CAI – Final medication option before resorting to laser or incisional surgical treatment

Carbonic anhydrase Inhibitors (CAI)

Side effects

Paresthesia
Frequent urination
GI disturbances
Hypokalemia

Topical Miotics

- Only of historical importance in open angle glaucoma
- - Ciliary muscle contraction
 - Increase drainage through trabecular meshwork
- Drug----Pilocarpine 1,2,4%.
- Less useful drug – Numerous side effects & three to four times a day dosing

Stepped Medical Approach to Treatment of Open Angle Glaucoma

Start monotherapy with **Latanoprost or topical β blocker**

If target I.O.P. not attained, either change over to alternative drug or use both the above concurrently

Brimonidine/dorzolamide – Use only when there are contraindications to PG analogs/ β blockers or to supplement their action

Oral acetazolamide/Topical miotics – Last resort

Angle closure Glaucoma

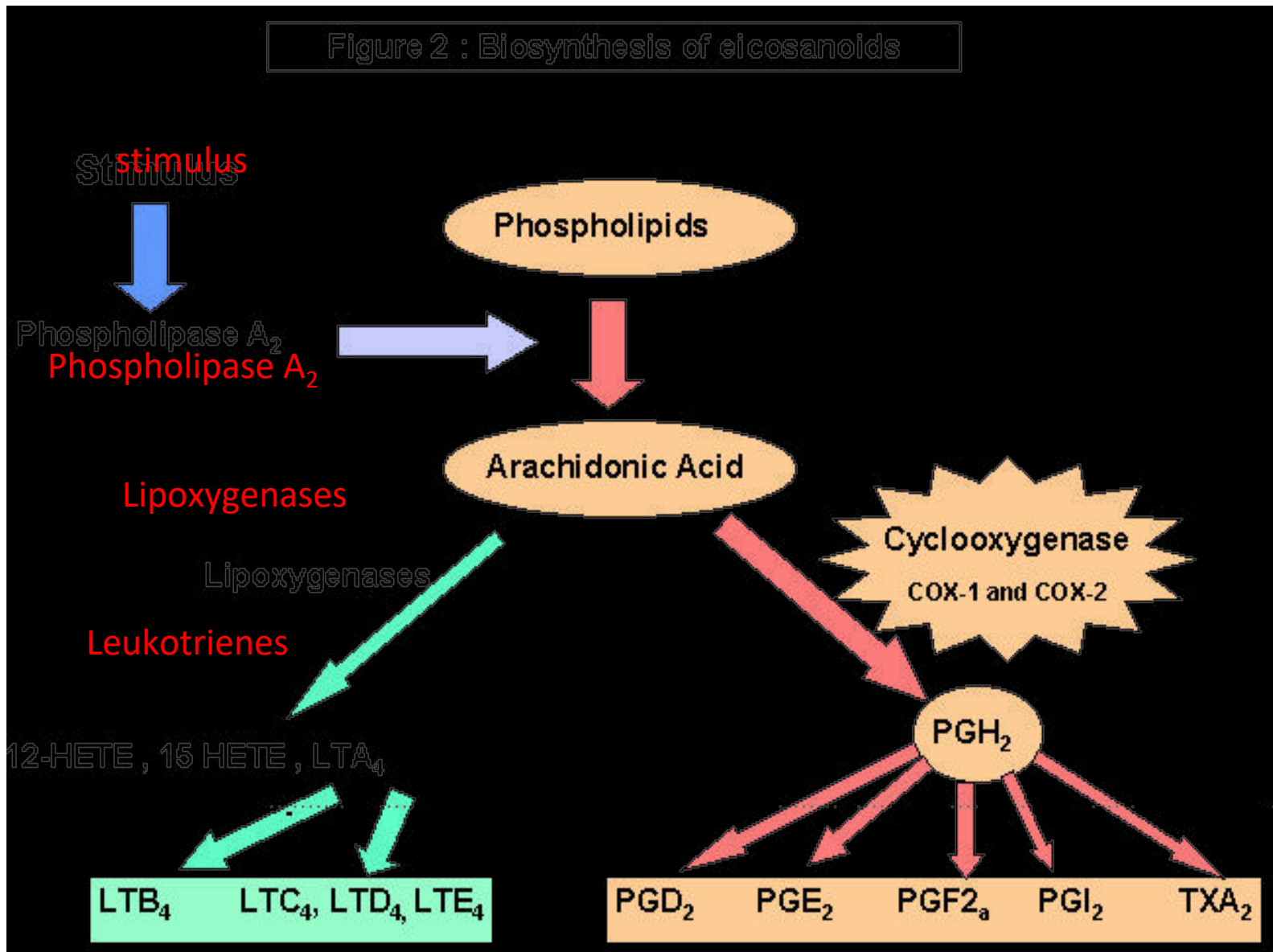
1. Hypertonic Mannitol (20%)
IV infusion 1.5 -2 g/kg
2. Acetazolamide - 0.5 g oral
3. Miotic - Pilocarpine (1-4%)
4. Timolol 0.5 % - instilled 12 hourly.

**Definitive treatment – Surgical/
Laser iridotomy**

**Anti-
inflammatory**

Corticosteroid

NSAID



Corticosteroids

CLASSIFICATION

Short acting

Hydrocortisone, Cortisone, Prednisolone

Intermediate acting

Triamcinolone, Fluprednisolone

Long acting

Dexamethasone, Betamethasone

Therapeutic Uses of Topical steroids

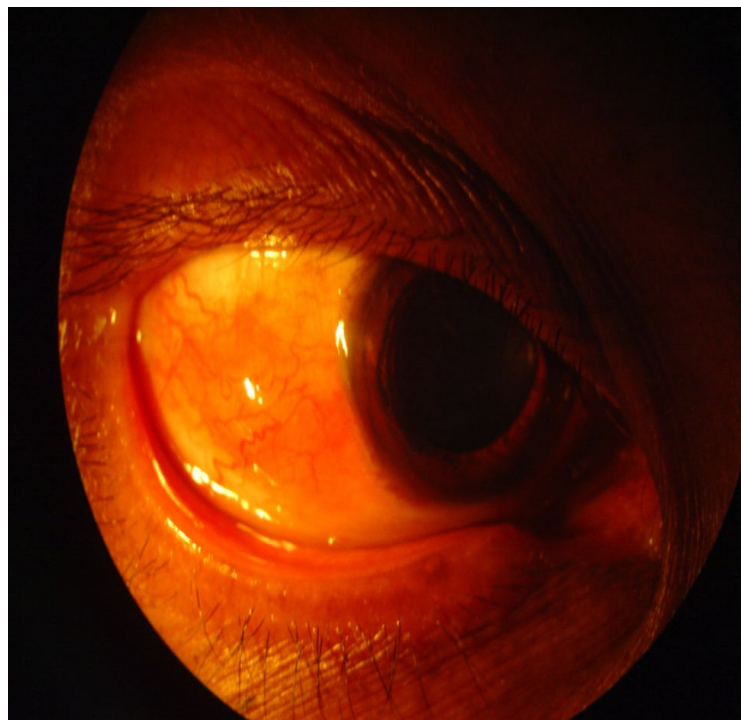
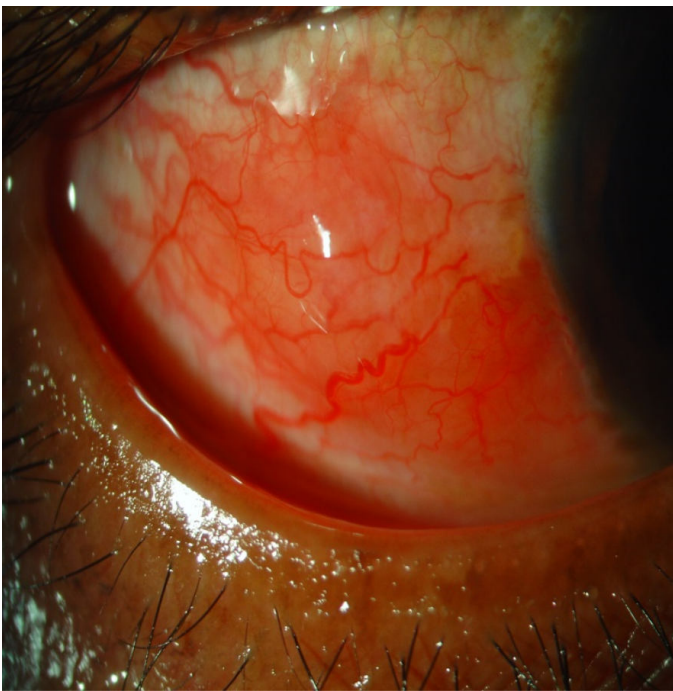
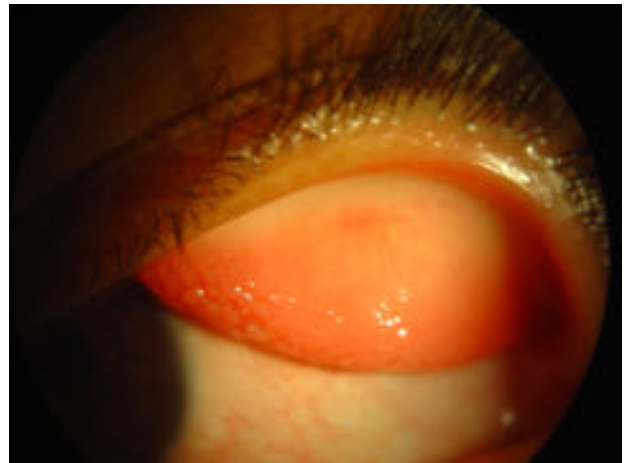
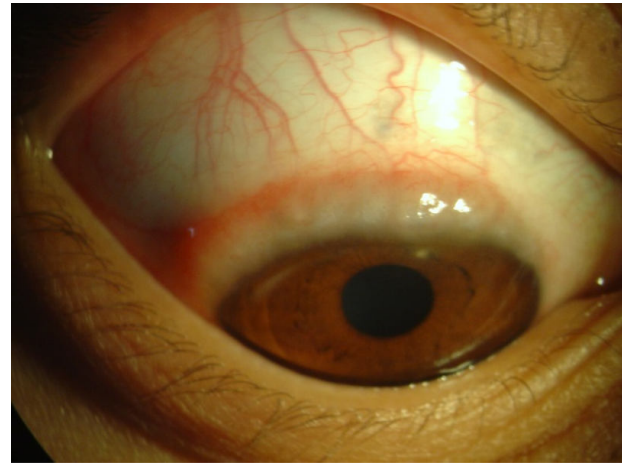
1. Significant ocular allergy
2. Anterior uveitis
3. Postoperative inflammation following refractive, corneal & intraocular surgery
4. To reduce potential scarring of surgical site (After Glaucoma filtering surgery)

NEVER GIVE STEROIDS IF YOU ARE SUSPECTING ACTIVE INFECTION

Steroids in ocular conditions.....

- Systemic steroids & by sub-Tenon's capsule injection – Posterior Uveitis
- **Intravitreal injection** –
 - Age-related Macular degeneration (ARMD)
 - Diabetic Retinopathy
 - Cystoid Macular Edema (CME)
- **Parenteral steroids** followed by tapering oral doses
 - Optic Neuritis

ALLERGIC CONJUNCTIVITIS

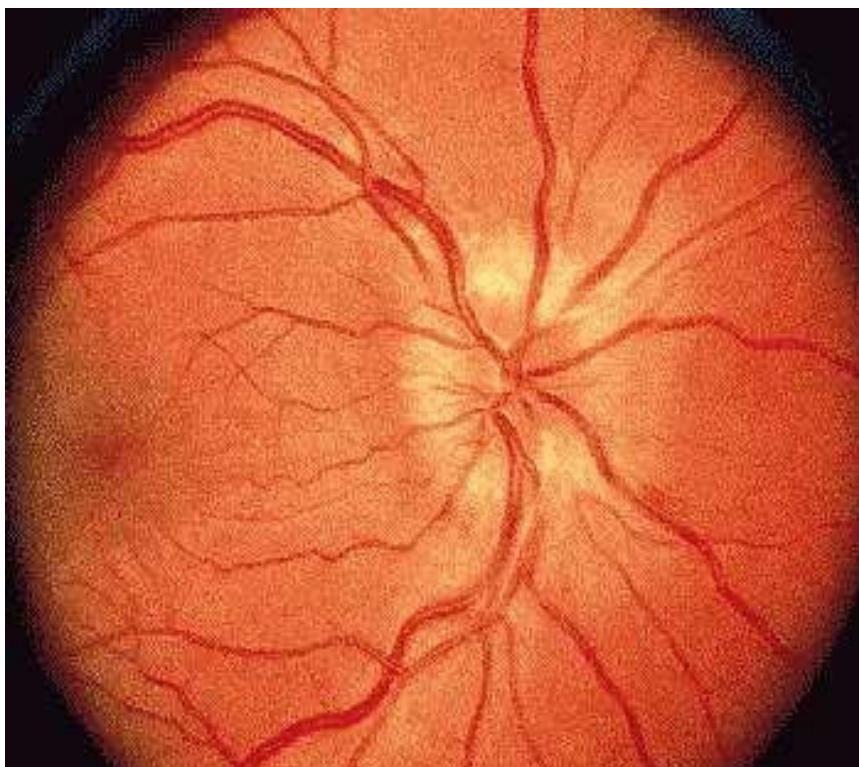


SCLERITIS





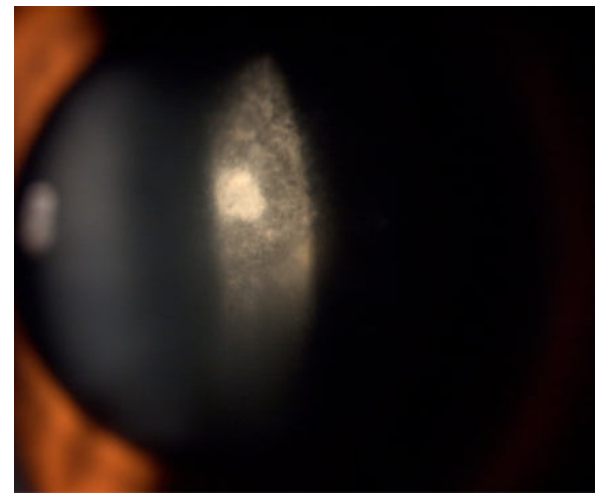
ANTERIOR UVEITIS



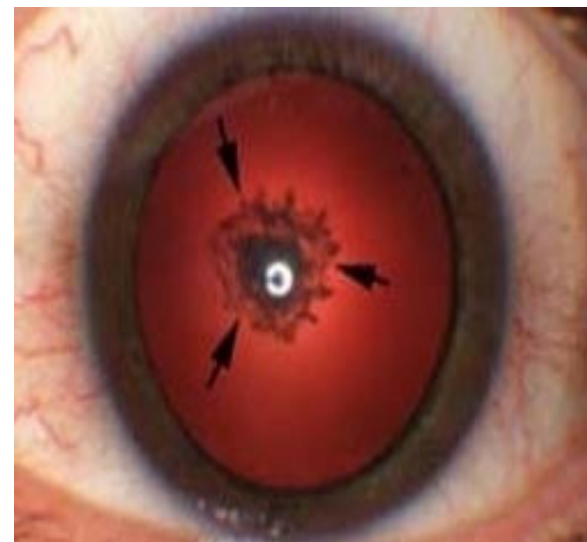
OPTIC NEURITIS

Toxicity of Steroids

1. Posterior subcapsular cataracts
2. Secondary infections
3. Secondary open-angle glaucoma
4. Delayed wound healing



*“ Soft steroids (e.g., Loteprednol)
reduce the risk of elevated IOP ”*



SYSTEMIC side effects of steroids

Peptic ulcer

Hypertension

Increased blood sugar

Osteoporosis

Mental changes

Activation of tuberculosis and other infections

Topical NSAIDs & their Ocular Uses

Sr. No.	Topical NSAID	Ocular Use
1	Flurbiprofen	To counter unwanted intraoperative miosis during cataract surgery
2	Ketorolac	-Seasonal allergic conjunctivitis -Cystoid Macular Edema (CME) occuring after cataract surgery
3	Diclofenac	-Postoperative inflammation -Cystoid Macular Edema (CME) occuring after cataract surgery
4	Bromfenac	Postoperative pain & inflammation after cataract surgery
5	Nepafenac	Postoperative pain & inflammation after cataract surgery

Tear Substitutes

- Hypotonic or isotonic solutions –
 - Eg: Carboxymethylcellulose
 - Polyvinyl alcohol
 - Polyethylene and propylene glycol
- **Indications**
 - Ocular irritation in various diseases
 - Dry eye disease

Therapeutic Uses of Tear Substitutes

- Ocular diseases
 - Allergic conjunctivitis
 - Blepharitis
 - Corneal dystrophies
 - Chemical Burns

- Systemic diseases
 - Sjogren's syndrome
 - Rheumatoid arthritis
 - Vitamin A deficiency
 - Stevens-Johnson syndrome

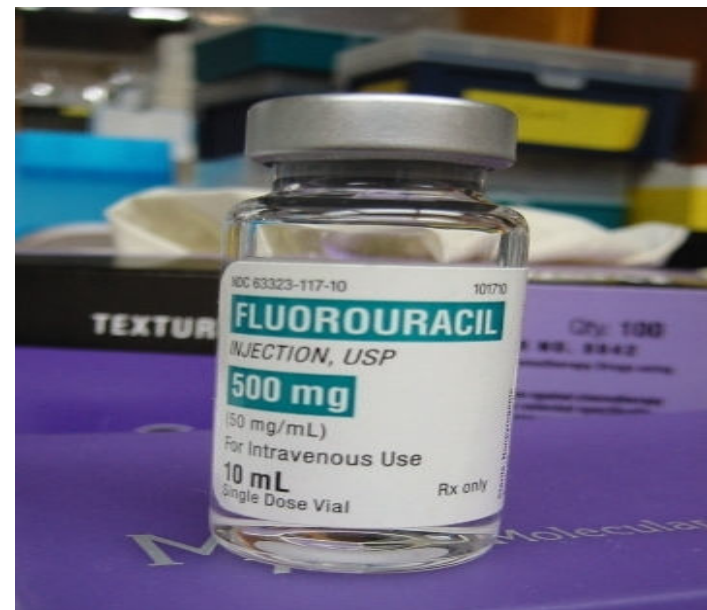
Immunosuppressive & Antimitotic Agents

Agents commonly used –

1. 5-fluorouracil
2. Mitomycin C

Used

- In Glaucoma surgery, to improve success of filtration surgery by limiting postoperative wound-healing process.
- In corneal surgery, to reduce risk of scarring after excision of pterygium



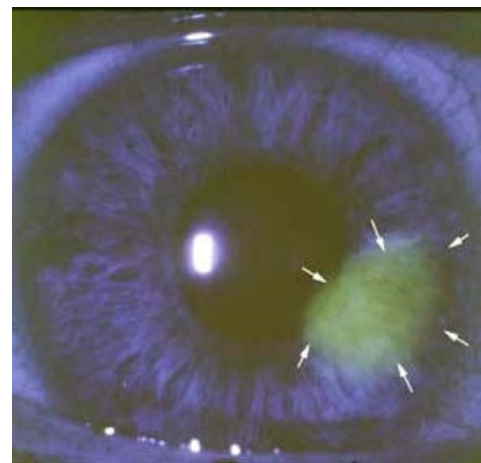
Immunomodulatory Agent

Topical Cyclosporine

- Approved for the treatment of chronic dry eye associated with inflammation
- Decreases inflammatory markers in lacrimal gland & **increases tear production**

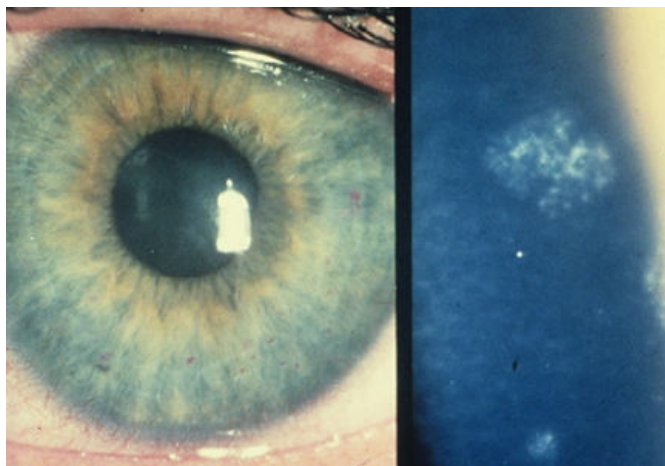
Ocular diagnostic drugs

- Fluorescein dye
 - Available as drops or strips
 - **Uses:**
 - To stain corneal abrasions
 - applanation tonometry
 - detecting wound leak
 - fluorescein angiography
 - **Caution:**
 - Stains soft contact lens
 - Fluorescein drops can be contaminated by *Pseudomonas* sp.



Ocular diagnostic drugs

- Rose bengal stain
 - Stains devitalized epithelium
 - **Uses:** severe dry eye, herpetic keratitis



Anaesthetics In Ophthalmic Procedures

- Proparacaine & tetracaine drops –
 - Uses – Tonometry
 - Gonioscopy
 - Removal of foreign bodies, sutures on conjunctiva and cornea
- **Adverse effects:** toxic to corneal epithelium
allergic reaction (rarely)

Drugs & Biological Agents Used in Ophthalmic Surgery

Sr. No.	Drugs & Biological Agents	Use in Ophthalmic Surgery
1	Povidone iodine (5% solution)	To prepare periocular skin & to irrigate cornea, conjunctiva & palpebral fornices
2	Viscoelastic substances (chondroitin sulphate, hydroxypropylmethylcellulose)	Maintain spaces & protects surfaces during anterior segment surgery
3	Ophthalmic Glue- a) Cyanoacrylate tissue adhesive b) Fibrinogen Glue	Corneal ulcerations & Perforations To secure conjunctiva & corneal grafts.
4	Anterior Segment Gases a) Sulfur Hexafluoride (SF6) b) Perfluoropropane	Reattachment of Descemet's membrane to stroma of Cornea
5	Vitreous Substitutes	Reattachment of retina following Vitrectomy.

Botulinum Toxin Type A

FDA approved - **Strabismus & Blepharospasm**
associated with dystonia, facial wrinkles (glabellar lines), axillary hyperhydrosis & spasmodic Torticolis

MOA – Prevention of acetyl choline release at neuromascular junction – temporary paralysis of locally injected muscle

Ophthalmic Effects of Selected Vitamin Deficiencies & Zinc Deficiency

Deficiency	Effects in Anterior Segment	Effects in Posterior Segment
Vitamin A	Conjunctiva(Bitot's spot, xerosis) Cornea (Keratomalacia , Punctate keratopathy)	Retina(Nyctalopia) Retinal pigment epithelium (hypopigmentation)
Vitamin B1	----	Optic nerve (Visual field defects)
Vitamin B6	Cornea(Neovascularization)	Retina (Atrophy)
Vitamin B12	-----	Optic nerve (Visual field defects)
Vitamin C	Lens (? Cataract formation)	-----

Ophthalmic Effects of Selected Vitamin Deficiencies & Zinc Deficiency

Deficiency	Effects in Anterior Segment	Effects in Posterior Segment
Vitamin E	-----	Retina & retinal pigment epithelium (? Macular degeneration)
Folic acid	-----	Vein occlusion
Vitamin K	Conjunctiva (Hemorrhage)	Retina (Hemorrhage)
Zinc	-----	Retina & retinal pigment epithelium (? Macular degeneration)

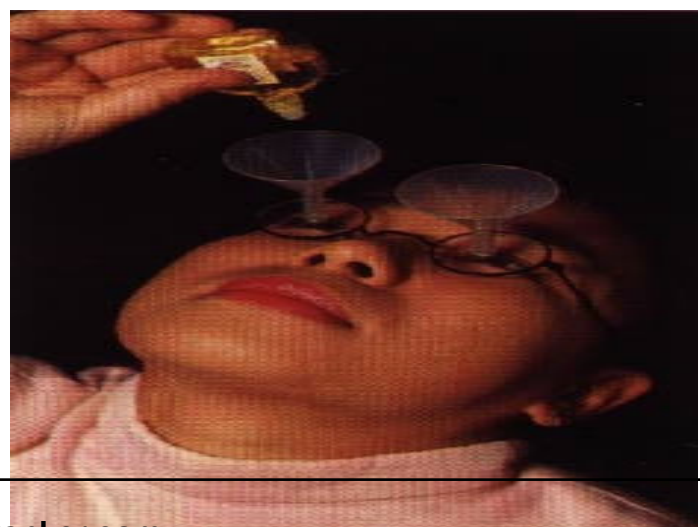
Ocular Toxicology

Toxicology

- All ophthalmic medications – Potentially absorbed into systemic circulation – Undesirable systemic side effects
- Eg. Timolol (single eye drop) - Death
- Local toxic effects – Hypersensitivity reactions
- Preservatives in eye drops & contact lens solutions –
 1. Benzalkonium chloride – Punctate Keratopathy
 2. Thimerosal – Hypersensitivity reactions

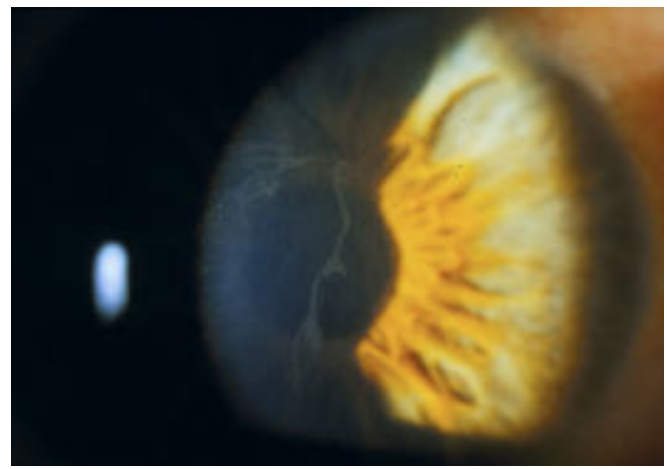
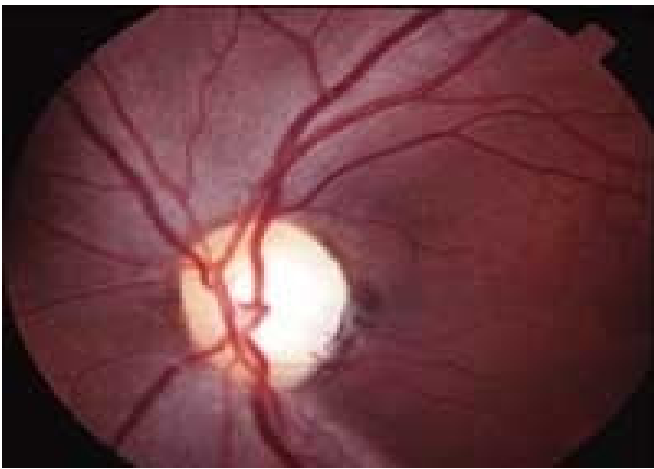
Complications of topical administration

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



Amiodarone

- A drug for treatment of cardiac arrhythmia
- Causes **optic neuropathy** (mild decreased vision, visual field defects, bilateral optic disc swelling)
- Also causes corneal vortex keratopathy (corneal verticillata) which is whorl-shaped pigmented deposits in the corneal epithelium



Digitalis

- A drug for treating cardiac failure
- Causes **chromatopsia** (objects appear yellow) with overdose



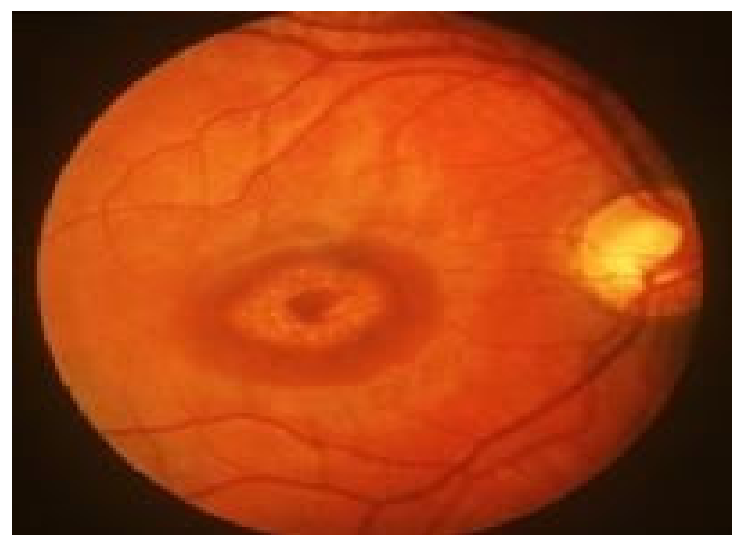
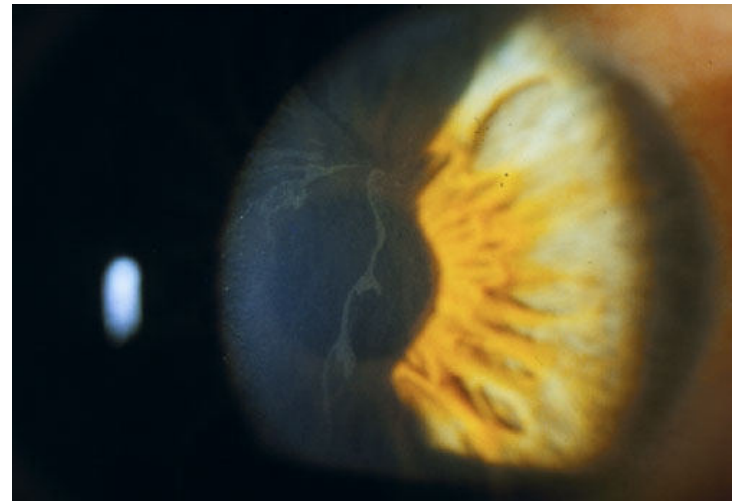
French market scene viewed with no color deficiency



French market scene viewed with xanthopsia

Chloroquines

- E.g. chloroquine, hydroxychloroquine
- Used in malaria, rheumatoid arthritis, SLE
- Cause vortex keratopathy (corneal verticillata) which is usually asymptomatic but can present with glare and photophobia
- Also cause **retinopathy** (bull's eye maculopathy)

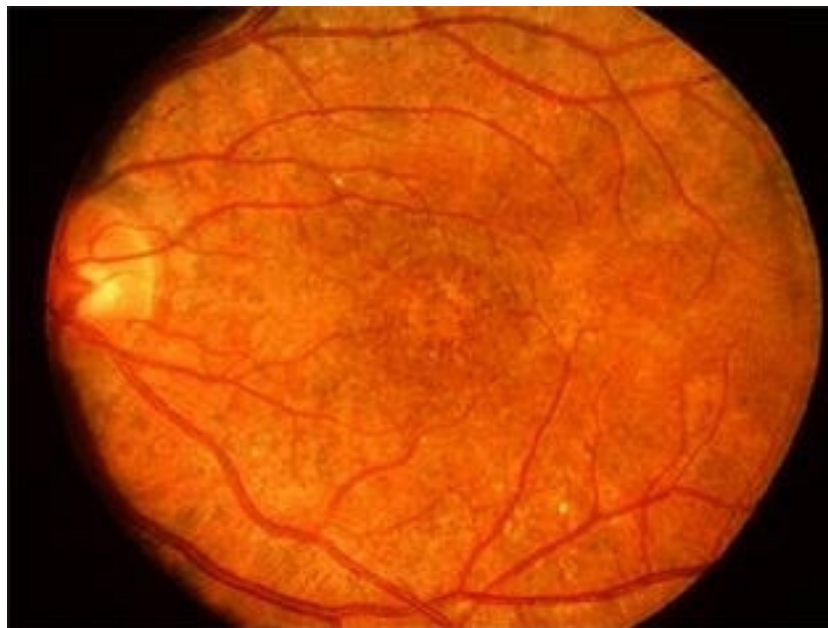


Chorpromazine

- An antipsychotic drug
- Causes **corneal punctate epithelial opacities, lens surface opacities**
- Rarely symptomatic
- Reversible with drug discontinuation

Thioridazine

- A psychiatric drug
- Causes a **pigmentary retinopathy** after high dosage

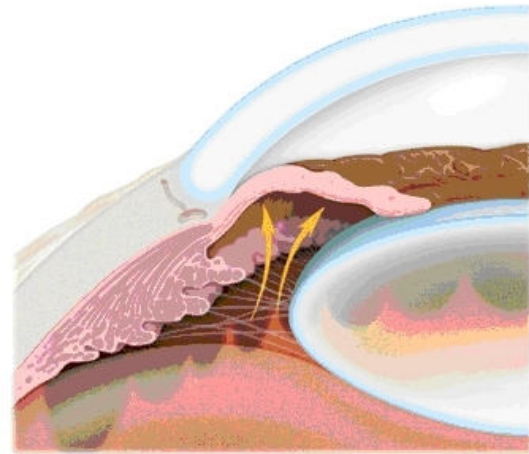


Diphenylhydantoin

- An epilepsy drug
- Causes dosage-related cerebellar-vestibular effects:
 - Horizontal **nystagmus** in lateral gaze
 - Diplopia, ophthalmoplegia
 - Vertigo, ataxia
- Reversible with discontinuation of the drug

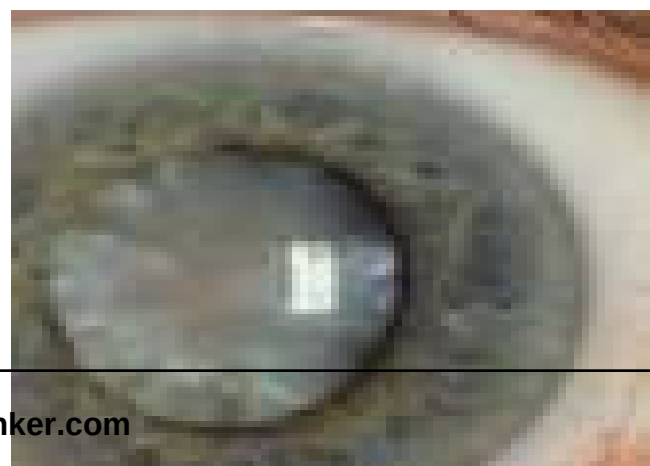
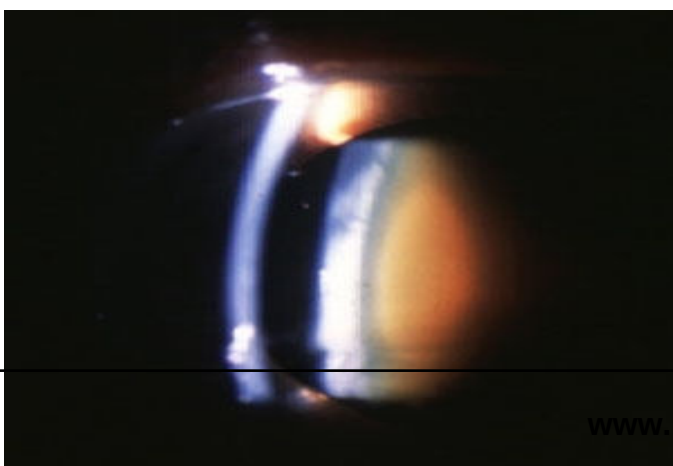
Topiramate

- A drug for epilepsy
- Causes **acute angle-closure glaucoma** (acute eye pain, redness, blurred vision, haloes).
- Treatment is by **cycloplegia and topical steroids** (rather than iridectomy) with the discontinuation of the drug



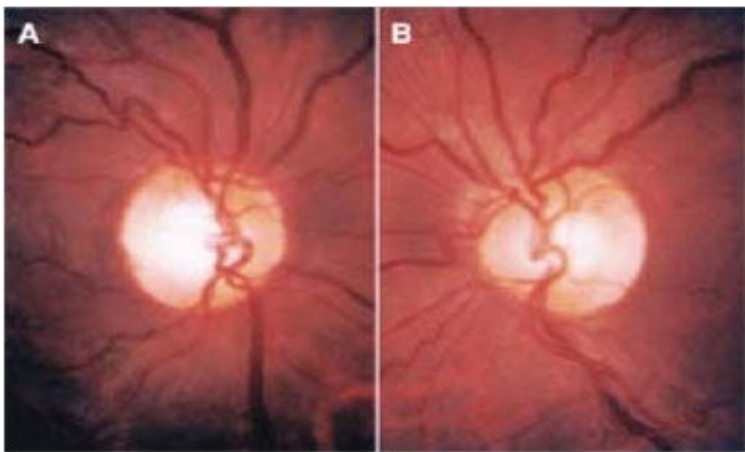
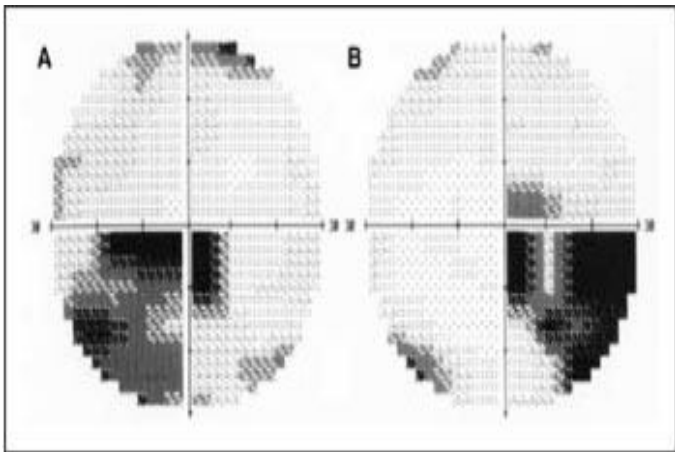
HMG-CoA reductase inhibitors (statins)

- Cholesterol lowering agents
- E.g. pravastatin, lovastatin, simvastatin, fluvastatin, atorvastatin, rosuvastatin
- Can cause **cataract** in high dosages specially if used with erythromycin



Ethambutol

- An anti-tubercular drug
- Causes a dose-related **optic neuropathy**
- Usually reversible but occasionally permanent visual damage might occur



Systemic Agents with Ocular Side Effects

Sr. No.	Name of Drug	Ocular Side Effect
1.	Topiramate	Angle Closure Glaucoma
2.	Hydroxychloroquine/Chloroquine	Chloroquine amblyopia (Bull’s Eye Maculopathy)
3.	Tamoxifen	Crystalline Maculopathy
4.	Vigabatrin	Progressive & Permanent bilateral concentric visual field constriction
5.	Sildenafil/Vardenafil/tadalafil	Nonarteritic Ischemic Optic Neuropathy (NAION)
6.	Ethambutol, Chloramphenicol , Rifampin	Toxic Optic Neuropathy (Progressive bilateral central scotomas & vision loss)
7.	Ocular Steroids	Elevated IOP & Glaucoma
8.	Steroids	Cataract

Systemic Agents with Ocular Side Effects.....

Sr. No.	Name of Drug	Ocular Side Effect
9.	Rifabutin + Clarithromycin / Fluconazole	Iridocyclitis & Hypopyon
10.	Isotretinoin	Dry eye & meibomian gland dysfunction
11.	Amiodarone	Drug deposits in cornea (Cornea verticillata)
12.	Chlorpromazine & Thioridazine	Brown pigmentary deposits in the cornea
13.	Gold	Chrysiasis (gold deposits in cornea & conjunctiva)
14.	Tetracyclines	Yellow discoloration of light-exposed conjunctiva

Visual field constriction



Cataract



Thank you

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