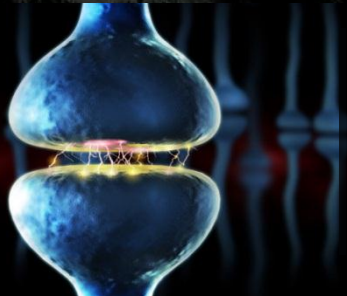
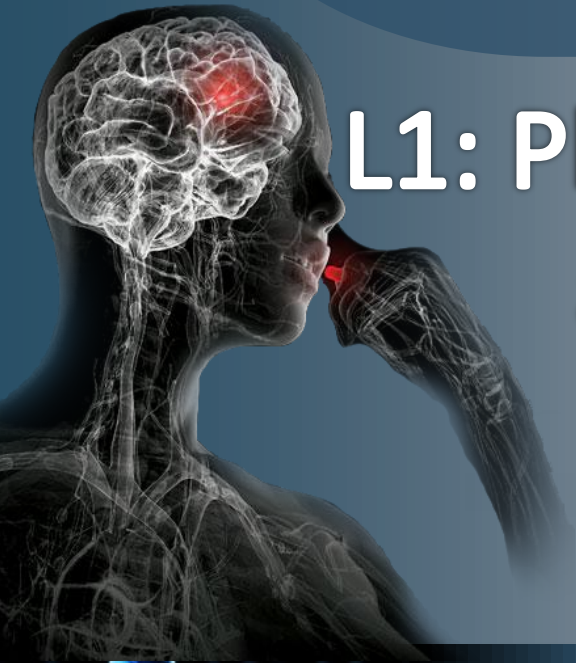


King Saud University
College of Medicine
2nd Year, 1st Block



L1: Pharmacology of drugs acting on the eye



CNS Block

remember

Structure	Sympathetic Stimulation	Parasympathetic Stimulation
Iris (eye muscle)	Pupil dilation	Pupil constriction
Salivary Glands	Saliva production reduced	Saliva production increased
Oral/Nasal Mucosa	Mucus production reduced	Mucus production increased
Heart	Heart rate and force increased	Heart rate and force decreased
Lung	Bronchial muscle relaxed	Bronchial muscle contracted
Stomach	Peristalsis reduced	Gastric juice secreted; motility increased
Small Intes	Motility reduced	Digestion increased
Large Intes	Motility reduced	Secretions and motility increased
Liver	Increased conversion of glycogen to glucose	-----
Kidney	Decreased urine secretion	Increased urine secretion
bladder	Wall relaxed Sphincter closed	Wall contracted Sphincter relaxed



CNS Block

Routes of drug administration into the eye

Extra Intravitreal means administration within vitreous body of the eye while Intracameral is an intraocular route that begins in the ant chamber of the eyeball

Locally (Topically)
more common

Eye drops

most common

Their contract time is low to be used several times.

Ointment

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

Disadvantages:

The drug has to be high lipid soluble with some water solubility to have the maximum effect as ointment.

Injections

-Intraocular injections:

Intracameral or intravitrea.

-**Intracameral** acetylcholine (miochol) during cataract surgery.

-**Intravitreal** antibiotics in cases of endophthalmitis & steroid in macular edema.

-Peri-ocular injections:

-subconjunctival, peribulbar, or retrobulbar.

-reach behind iris-lens diaphragm better than topical application.

-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.

These routes can reach to the systemic circulation but it is less than IV, IM & Oral.

Routes of drug administration into the eye

Systemically

- 1) Oral
- 2) IV

-Factor influencing systemic drug penetration into ocular tissue:

***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.

Pharmacology of drugs acting on the eye

- 1) Drugs used for the treatment of eye.
- 2) Drugs that can produce harmful effects on the eye. (next slide)

1) Ophthalmic Uses of Drugs

a) Autonomic drugs:

* Affect the size of the pupil:

- Miotics
- Mydriatics

* Affect accommodation (Cycloplegics).

b) Anti-inflammatory drugs:

- Glucocorticoids
- NSAIDs

c) Chemotherapeutics (antibacterial, antifungal and antiviral agents).

d) Local Anesthetic drugs

2) Harmful drugs for the Eye

Drugs that ↑ IOP:

- Mydriatic cycloplegics.
- tricyclic antidepressants.
- Chronic steroid use.

Cataractogenic drugs:

- steroids.
- phenothiazines.
- heavy metals.

Drugs causing corneal deposits:

1-chloroquine, amiodarone.

-Amiodarone: a cardiac arrhythmia drug.

This drug causes optic neuropathy (mild decreased vision, visual field defects). Also causes corneal keratopathy which is pigmented deposits in the corneal epithelium.

2-Digitalis: cardiac failure drug.

Causes chromatopsia (objects appear yellow) with overdose.

Autonomic Nerve supply of the Eye

Parasympathetic N.S.

Constriction of the **pupillary sphincter** muscle (circular muscle)
(miosis)

Contraction of the **ciliary muscle**
(accommodation for near vision) M3

Decrease in intraocular pressure

Increased lacrimation

Conjunctival Vasodilatation

sympathetic N.S.

Contraction of **dilator Pupillae** (Iris radial muscle) **(Mydriasis)** α_1

Relaxation of **ciliary muscles**
(accommodation for far vision) β_2

Increase in intraocular pressure
(Narrow filtration angle)

Decrease Lacrimation α_1

Conjunctival Vasoconstriction α_1

a)Autonomic drugs

1)Cholinergic agonists

Drugs acting on parasympathetic system (**Miotics** drugs)

Cholinergic agonists	<ul style="list-style-type: none">-Direct agonists : (acting on the receptors) Pilocarpine, Methacholine, carbachol.-Indirect acting agonists : (anticholinesterases) Reversible :Physostigmine Irreversible: Ecothiophate
USES	<ul style="list-style-type: none">-Glaucoma (open angle glaucoma)-Counteract action of mydriatic-To break adhesions.-in accommodative esotropia (ecothiophate)
Adverse Effects	<ul style="list-style-type: none">-Miosis - Salivation - Sweating - bronchial constriction - vomiting – diarrhea.-CNS effects: high doses (physostigmine & pilocarpine)-Ocular side effects: diminished vision (myopia), headache
Contraindications	<p>Bronchial asthma -Peptic ulcer- Angina pectoris - Incontinence - Intestinal obstruction.</p>

a)Autonomic drugs

1)Cholinergic drugs

Drugs acting on parasympathetic system (Miotics drugs)

Drugs	uses
Acetylcholine Carbachol Methacholine (they use very limited)	Induction of miosis in surgery Glaucoma
Pilocarpine cross BBB = lipid soluble	In open angle glaucoma
Physostigmine cross BBB = lipid soluble	Glaucoma, accommodative esotropia
Ecothiophate dosen't cross BBB = water soluble	Glaucoma, accommodative esotropia

a)Autonomic drugs

2)Cholinergic antagonists (Muscarinic antagonists)

Divided into 2 groups

1- Natural alkaloids (e.g. Atropine, Scopolamine “hyoscine”)

2- Synthetic atropine substitutes (e.g. Homatropine, Cyclopentolate, Tropicamide)

Cholinergic antagonists	Effects	Uses	Side effects	Contraindications
	<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.▪ Loss of light reflex.▪ Increased i.O.P→ glaucoma.▪ ↓ Lacrimal secretion → sandy eye.	<ul style="list-style-type: none">-To prevent adhesion in uveitis & iritis.- Funduscopy examination of the eye.- Measurement of refractive error.	<ul style="list-style-type: none">-Blurred vision.-Tachycardia.-Constipation.-Urinary retention.-Dry mouth.-Sandy eyes.-Fever.CNS effects:-sedation.-hallucination.-excitation (toxic dose).	<ul style="list-style-type: none">-Glaucoma (angle closure glaucoma).-Tachycardia.-Prostate Hypertrophy.-Constipation.-Paralytic ileus.

a) Autonomic drugs

3) Adrenergic agonists

Drugs acting on sympathetic system (Mydriatics drugs)

	Non-selective agonists	α_1 agonists	α_2 agonists	β blockers
EXAMPLE	Epinephrine, depevefrin (pro-drug of epinephrine)	Phenylephrine	Apraclonidine (eye drops)	-Timolol, Carteolol. -Betaxolol (β_1)
Uses	Open angle glaucoma	-Fundusopic examination of the eye. -To prevent adhesion in uveitis & iritis . - Decongestant in minor allergic hyperemia of eye.	Glaucoma, prophylaxis against IOP spiking after glaucoma laser procedures	Open angle glaucoma
Mechanism	↑ Uveoscleral outflow of aqueous humor	-----	↓ Production of aqueous humor	↓ Production of aqueous humor
Side effect	Arrhythmia, tachycardia	May cause hypertension	Lethargy, fatigue, dry mouth	-----
Contra indications	Closed angle glaucoma	Closed angle glaucoma	-----	Asthmatic patients (less with betaxolol) , Cardiovascular patients Depression

Not important ;)

b) Anti-inflammatory drugs: **Corticosteroids**

Mechanism

- inhibition of arachidonic acid which released from phospholipids by inhibiting phospholipase A2

Topical

- prednisolone, dexamethasone, hydrocortisone
- Uses: postoperatively, anterior uveitis, severe allergic conjunctivitis, scleritis, prevention and suppression of corneal graft rejection

Systemic

- prednisolone, cortisone
- Uses: posterior uveitis, optic neuritis.

Side effects:

- Glaucoma, cataract, mydriasis
- Suppression of pituitary-adrenal axis
- Hyperglycemia, Osteoporosis
- Peptic ulcer, Psychosis, susceptibility to infections

b) Anti-inflammatory drugs:

NSAID

Not important ;)

Mechanism

- inhibition of cyclo-oxygenase
- E.g. ketorolac, diclofenac

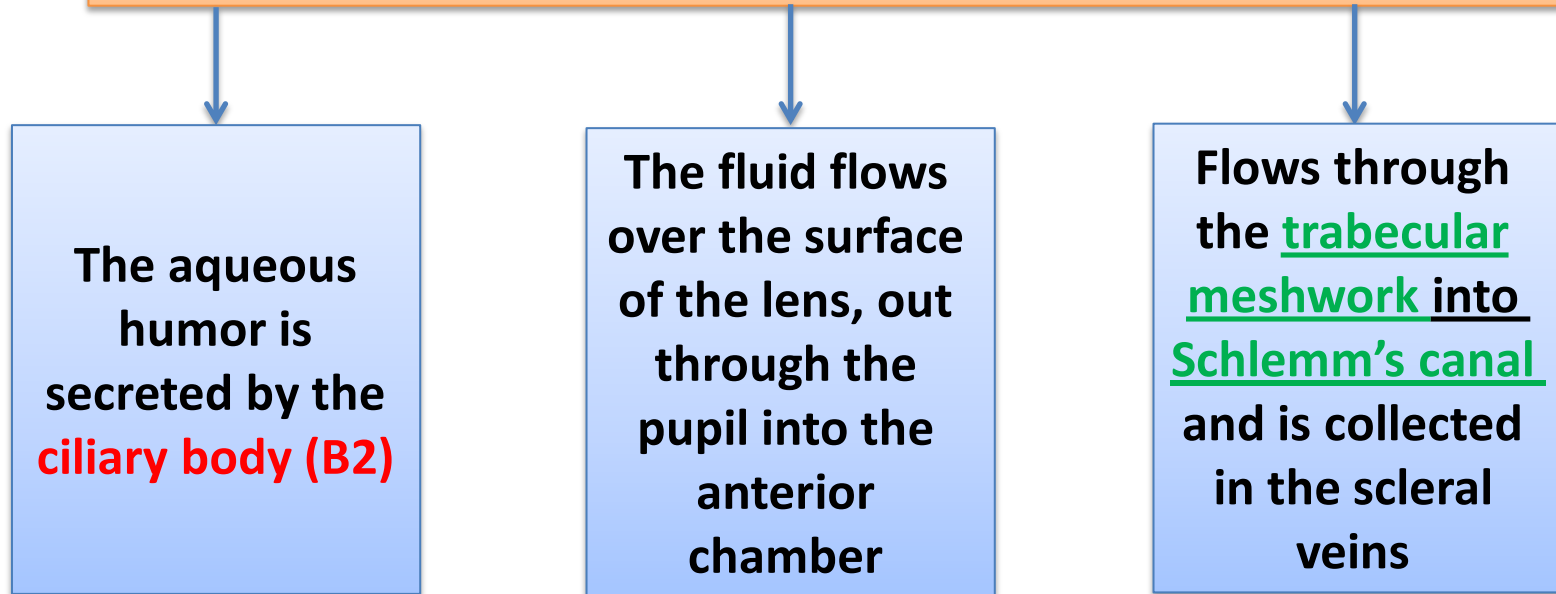
Uses

- postoperatively, mild allergic conjunctivitis, episcleritis, mild uveitis, cystoid macular edema, preoperatively to prevent miosis during surgery

Side effects

- stinging

Aqueous humor



How can we treat Glaucoma by ?

*by increasing the aqueous outflow through the trabecular meshwork canal of Schlemm by ciliary muscle relaxation α agonists.

* **β receptors** in the blood vessels of the ciliary processes \rightarrow \uparrow production of aqueous humour.

(so we can use **β antagonists** to \downarrow production of aqueous humour)

Treatment of glaucoma

<p><u>Chronic=open angle :</u></p> <p>The main goal is to decrease IOP, so :</p>		<p><u>Acute = closed or narrow angle:</u></p> <p>Is associated with occlusion of the outflow drainage pathway, Acute, painful increases of pressure</p>	<p><u>Osmotic agent:</u></p> <p>Dehydration which reduce IOP</p>
<p>By:</p> <p>Increasing outflow of aqueous humor</p>	<p><u>Or by:</u></p> <p>Decreasing production of aqueous humor</p>	<p>The use of drugs is limited to :</p> <ul style="list-style-type: none"> *Oral Acetazolamide. *Topical cholinomimetics e.g.: pilocarpine* *Dehydrating agents: IV infusion Of hypertonic solution (Mannitol, Glycerol). *Analgesics: pethidine or morphine (for pain). (in this case we must do operation) 	<p>glycerol 50% syrup cause: nausea, hyperglycemia.</p> <p>Mannitol 20% IV Cause: fluid overload and not used in heart failure</p>
<p>1- Prostaglandins.</p> <p>2- Adrenergic agonists, nonspecific</p> <p>3- Parasympathomimetics.</p>	<p>1- Beta blockers.</p> <p>2- Alpha-2 agonists.</p> <p>3-carbonic anhydrase inhibitors.</p>		

notes: for chronic IOP, the most popular drugs are Prostaglandins and Beta blockers.

ER situations require treatment before surgery e.g: **iridectomy.**

Carbonic anhydrase inhibitors

acetazolamide (oral)
dorzolamide (topical)

Prostaglandins

Latanoprost, travoprost
Are prostaglandins F_{2α} analogs
(Topical drops)

Mechanism:

↓ production of aqueous humor by blocks carbonic anhydrase enzyme required for production of bicarbonate ions (transported to posterior chamber, carrying osmotic water flow).

Side Effects (mainly with acetazolamide) :
myopia, malaise, anorexia, GI upset, headache
metabolic acidosis, renal stone
bone marrow suppression “aplastic anemia”

Contraindication:

sulpha allergy

Mechanism:

Increases uveoscleral outflow by relaxing ciliary body muscle

Side Effects:

Iris color change

Uses:

open angle glaucoma

Other agents which causes diseases to the eye

Drug	Causing
methanol	optic atrophy and blindness
Ethambutol	optic neuropathy
Hypervitaminosis A	yellow skin and conjunctiva, retinal hemorrhage
Hypovitaminosis A	night blindness (nyctalopia).

summary

Drug	Uses	S.E	Contraindications
Cholinergic agonists Direct agonists : Pilocarpine	Glaucoma (open angle glaucoma)	Ocular side effects: diminished vision (myopia), headache,	Bronchial asthma. Peptic ulcer. Angina pectoris
Non-selective agonists (α_1, α_2, β_1, β_2), eye drops Epinephrine	open angle glaucoma	cardiovascular arrhythmia, tachycardia	closed angle glaucoma in patients with narrow angles
α_1 agonists (phenylephrine)	Funduscopy examination of the eye prevent adhesion in uveitis - & iritis		closed angle glaucoma in patients with narrow angles
α_2 agonists (apraclonidine)	glaucoma treatment, prophylaxis against IOP spiking after glaucoma laser procedures	Lethargy, fatigue, dry mouth	
β blockers (can be used in patients with hypertension/ischemic heart disease)	open angle glaucoma		Bronchospasm (less with betaxolol) bradycardia, hypotension, asystole, syncope
Carbonic anhydrase inhibitors (acetazolamide (oral), dorzolamide (topical))	↓ production of aqueous humor	renal stone	sulpha allergy
Prostaglandins (Latanoprost, travoprost)	open angle glaucoma	Iris color change	

M C Q S

1- Factor influencing systemic drugs penetration into ocular tissue :

- A- lipid solubility .
- B- Protein binding.
- C- Eye inflammation.
- D- All above.

2- Cholinergic agonists contraindicated in :

- A- Tachycardia.
- B- Paralytic ileus.
- C- Bronchial asthma.
- D- Prostate hypertrophy.

3- Used in accommodative esotropia :

- A- Ecothiophate.
- B- Cortisone.
- C- Atropine.
- D- Epinephrine.

4- Topical corticosteroids (E.g. prednisolone) is used for :

- A- Anterior uveitis.
- B- Severe allergic conjunctivitis.
- C- Prevention of corneal graft rejection.
- D- All above.

1=D, 2=C, 3=A, 4=D, 5=D, 6=B, 7=D

5- Drug causing corneal deposits:

- A- Chloroquine.
- B- Pilocarpine
- C- Amiodarone.
- D- A&C.

6- Non-selective adrenergic agonists & α_1 agonists are Contraindicated in :

- A- Open angle glaucoma.
- B- Close angle glaucoma.
- C- Severe allergic conjunctivitis.
- D- Uveitis

7- Corticosteroids side effects :

- A- Suppression of pituitary-adrenal axis.
- B- Hyperglycemia.
- C- optic neuritis.
- D- A&B.

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**We hope that we made this lecture easier for you
Good Luck !**



CNS Block