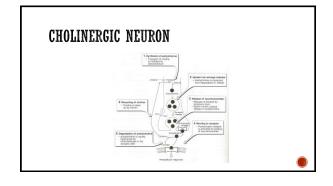
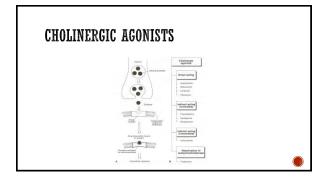


# CHOLINERGIC DRUGS - Direct agonists - Indirect agonist - Antagonist - Antagonist - Antagonist - College drugs Chinad buse Control - Receptor IO buse Control - Receptor II support ample - Recept





## Direct agonist: Miosis, accomodation Increase aqueous outflow decrease IOP Acetycholine 1% carbachol 0.01% intracameral use constrict pupil anterior segment surgery - Acetycholine rapid effect but short lived - Carbachol 100 times more effective longer lasting 24 hours and decreases IOP

#### CHOLINERGIC DRUGS DIRECT AGONIST

- · Pilocarpine:
- lowers IOP by increasing outflow
- Open angle glaucoma treatment
- Side effects
- Miosis older patients with cataract difficulty in scotopic conditions
- Cataractogenesis
- Induced myopia and accommodation problems for younger patients; slow dissolving pilocarpine gel at bedtime

### CHOLINERGIC DRUGS: INDIRECT AGONIST CHOLINERSTERASE INHIBITORS

- · Phospholine iodide
- No longer available for ophthalmic use in US
- More potent than direct acting use twice a day
- Physostigmine, neostigmine, edrophonium

#### CHOLINERGIC ANTAGONISTS

- Atropine: post-synaptic blockage of acetylcholine
- Pupil dilation, cycloplegia for iritis, accurate cycloplegic refraction
- Treat malignant glaucoma
- Systemic atropine given during ophthalmic surgery involving EOM manipulation to block oculocardiac reflex and prevent bradycardia and hypotension
- Side effects of systemic absorption of atropine eye drops:
- Side effects treated with physostigmine
- Other antagonists: tropicamide, cyclopentolate, homatropine, scopolamine, Flushing, tachycardia, constipation, urinary retention, delirium.

#### INDIRECT ACTING ANTAGONIST

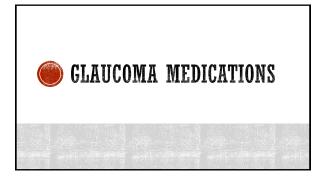
- Edrophonium test: increases acetylcholine at neuromuscular junction
- Myasthenia gravis: antibodies to acetylcholine receptor resulting in generalized weakness, ptosis and diplopia
- Edrophonium used to diagnose myasthenia gravis
- Neostigmine can be given IM for the same purpose and has a longer duration of activity
- \*Allows clinician more time to make orthoptic measurement for desired endpoint

### NEUROMUSCULAR BLOCKADE FOR GENERAL ANESTHESIA

- Globe laceration repair under general anesthetic
- Use of neuromuscular blocking drugs by anesthetist; i.e. succinylcholine is a "depolarizing" neuromuscular blocker and can cause contraction of EOMs on induction of general anesthetic and should not be used
- Exert force on open globe
- increase IOP in other cases where pressure measurement is desired such as in an examination under anesthesia

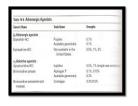
#### MYDIATICS AND CYCLOPLEGICS

| Generic Name  | and Cycloplegics   | Streogths  | Organi     | Darotion<br>of Arthur |
|---|--|--|------------|-----------------------|
| Phenylephrine HCI                                   | AX-Dilate<br>Altafrin<br>Mydfrin<br>Neofrin<br>Neo-Synephrine<br>Available generically | Bolution, 2.6%, 10%<br>Solution, 2.6%, 10%<br>Bolution, 2.6%<br>Solution, 2.6%<br>Solution, 2.6%<br>Solution, 2.8%<br>Solution, 2.8% | 30-60 min  | 3-5 h                 |
| hydroxyamphetamine<br>hydrotysenide, 1%             |  | Acceptable as powder for compounding   | 30-60 min  | 3-6 H                 |
| Atropine suffate                                    | Atropine Care<br>teopto Atropine<br>Available generically                              | Solution, 1%<br>Solution, 1%<br>Solution, 1%<br>Climmant, 1%   | 45-125 min | 7-14 day              |
| Cyclopentolate HCI                                  | AK-Pontolate<br>Cyclogyl<br>Cylate<br>Available penerically                            | Solution, 1%<br>Solution, 0.5%-2%<br>Solution, 1%<br>Solution, 1%, 2%  | 30-60 min  | 2 days                |
| hydrobsomide  | Homatropine<br>Homatropaire  | Solution, 2%, 5%<br>Solution, 5%   | 30-60 min  | 3 theys               |
| Scopolarnine<br>hydrotromide                        | Isopto Hyascine  | Solution, 0.25%  | 30-60 min  | 4-7 stays             |
| Tropicamide   | Mydral<br>Mydriacyl<br>Tropicacyl<br>Aradable generically                              | Solution, 0.5%, 1%<br>Solution, 1%,<br>Solution, 0.8%, 1%<br>Solution, 0.8%, 1%  | 20-40 min  | 4-6 h                 |
| Cyclopentalate HCI/<br>phenylephrine HCI*           | Cyclorrydrii   | Solution, 0.2%/1%  | 30:80 mm   | 1-2 days              |
| Hydroxyamphetamina<br>hydrotxomide/<br>tropicamide/ | Paramyd  | Selution, 1950,25%   | 20-40 min  | 4-61                  |



#### ADRENERGIC DRUGS

- · Norepinephrine (NE) is transmitter
- Alpha and beta receptors for NE
- · Direct agonists
- Indirect agonist
- antagonists



#### ALPHA-ADRENERGIC DRUGS

- Alpha-l phenylephrine Mydriasis stimulate iris dilator muscle
- Naphazoline: decongestant with rebound vasodilation and hyperemia
- · Elevate systemic blood pressure
- Caution: using 10% phenylephrine topically 5mg per drop; MI, stroke, cardiac arrest risks
- Systemic "pressor" dose bolus IV 50-100µgram



#### ALPHA-2 ADRENERGIC AGONISTS

- Apraclonidine (Iopidine)
   Pre and post YAG cap and SLT, cataract extraction to manage increased IOP

- increased IOP

  Prevents NE release decrease
  pupil size

  Decreases aqueous production
  and increases outflow

  Topical sensitivity 40% and
  tachyphylaxis limit long term
  use
- Brimonidine (Alphagan)Topical sensitivity 15%
- 0.2% with BAK
- 0.15% with polyquad
   0.1% with sodium chlorite preservative Purite Alphagan-P
- Avoid in infants less than 2 years: hypotension, hypothermia, bradycardia
- CNS effects resulting from medication crossing the blood-brain barrier

#### **ALPHA-2 ADRENERGIC AGONISTS**

- Caution in patients using apraclonidine or brimonidine :
- Patients taking systemic MAO inhibitors or tricyclic antidepressants
- Hypertensive risks

#### INDIRECT ACTING ADRENERGIC AGONISTS

- Cocaine 4% or 10%
- Hydroxyamphetamine 1%
- Office diagnostic testing to confirm Horner syndrome
- Available through compounding pharmacies

#### BETA-ADRENERGIC AGONISTS

- Epinephrine not available for glaucoma treatment
- •Dipiveprin (Propine) 0.1% available as generic
- Reduce aqueous production and increase trabecular outflow
- Reduced effectiveness over time

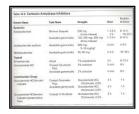
#### BETA-ADRENERGIC ANTAGONIST: BETA **BLOCKERS**

- Reduce aqueous production by up to 50%
- Inhibit the normal physiological responses of increasing pulse and BP with exertion: may be poorly tolerated in active or elderly with routine activities
- Induce bronchospasm in asthma and COPD patients
- Betaxolol selective β-1 inhibitor;
   0.5% solution or 0.25% suspension (Betoptic S) less irritating
- Nonselective β blockers:
- · Carteolol (Ocupress)
- Levobunolol (Betagan) Metipranolol (Optipranolol)
- · Timolol maleate (Timoptic)
- Timolol hemihydrate (Betimol)

#### BETA-ADRENERGIC ANTAGONISTS

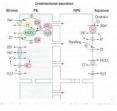
Strengths
0.25%
0.5%
1%
1%
0.25%, 0.5%
0.25%, 0.5%
0.3%
0.3%
0.3%
0.5%, 0.5%
0.5%, 0.5%

#### CARBONIC ANHYDRASE INHIBITORS



- Carbonic anhydrase is enzyme involving the production of aqueous humor in the ciliary body
- Topical preparations for Glaucoma treatment
- Acetazolamide (Diamox) oral in the management of pseudotumor cerebri

#### CARBONIC ANHYDRASE AND AQUEOUS **HUMOR SECRETION**



#### CARBONIC ANHYDRASE INHIBITORS

#### Topical:

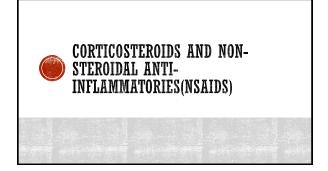
- Dorzolamide (Trusopt); In combination with Timolol (Cosopt)
- Brinzolamide (Azopt)

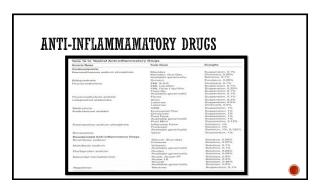
- Acetazolamide 4 times daily Methazolamide twice daily
- Side-effect is a systemic metabolic acidosis
- Low potassium may also result
- Renal stone formation 11 times higher
- Numbness and tingling hands and feet, weight loss from anorexia
- Skin rash

## PROSTAGLANDIN ANALOGUES

#### PROSTAGLANDIN ANALOGUES

- Latanoprost (Xalatan)
- Bimatoprost (Lumigan)
- Travoprost (Travatan)
- Tafluprost (Zioptan)
- Unoprostone (Rescula)
- Ocular side effects: darkening of iris and periocular skin
- · Hypertrichosis of eyelashes
- · Cystoid macular edema(CME)
- · Conjunctival hyperemia
- Reactivation of HSV keratitis
- Use with caution in pregnant patients since uterine contractions are mediated by prosaglandins





#### OCULAR ANTI-INFLAMMATORY DRUGS

#### **Routes of Administration**

- Local injection
- Ocular implantation
- Topical
- Systemically

#### Categories

- Glucocorticoids
- Non-steroidal antiinflammatory drugs
- Mast cell stabilizers
- Antihistamines
- Antifibrotics

#### GLUCOCORTICOIDS/STEROIDS

- Most important effect is inhibition of arachidonic acid (AA)
- AA is converted into potent mediators of inflammation:
- prostaglandins
- endoperoxidases
- leukotrienes thromboxanes
- Adverse ocular effects from topical steroids:
- Glaucoma
- Posterior subcapsular cataract
- Bacterial, viral infections increase
- Fungal infection
- Ptosis
  Cleral melt
- Eyelid skin atrophy

## STEROIDS ADVERSE EFFECTS: SYSTEMIC ADMINISTRATION

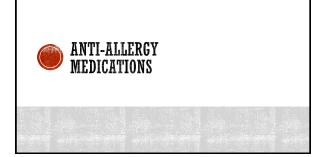
- · Suppression of pituitary-adrenal axis
- · Hyperglycemia, muscle-wasting, osteoporosis
- Redistribution of fat from periphery to trunk
- Euphoria
- Insomnias
- · Aseptic necrosis of the hip
- · Peptic ulcer
- Diabetes mellitus
- psychosis

#### STEROID-INDUCED ELEVATION OF IOP

- 4% develop an IOP > than 31 mm Hg after 6 weeks
- Reduce aqueous outflow is cause of IOP rise
- Dexamethasone>prednisolone>FML
- Reversible upon discontinuation of the drug if use is less than one year
- Permanent elevations of IOP if used more than 18 months
- Loteprednol 0.2%, 0.5% have lower incidences of increased IOP
- Fluocinolone implant for chronic uveitis
- Triamcinolone 40mg/ml preservative free for intravitreal use: increased rates of cataract and need for glaucoma treatment

## NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS)

- $\bullet$  Flurbiprofen 0.3% (Ocufen) first available topical NSAID used preop to reduce intraoperative miosis for cataract surgery
- Diclofenac 0.1% (Voltaren) prophylaxis and treatment of post-op inflammation and CME
- ${\mbox{\bf Ketorolac}}$  (Acular) post-op inflammation and allergic conjunctivitis treatment
- Nepafenac (Nevanac), Bromfenac (Xibrom) twice daily dosing treating postop cataract and retinal surgery inflammation
- NSAIDS have topical anesthetic properties: useful in short term management of: corneal abrasion, anterior segment procedures and refractive surgery



## ANTI-ALLERGIC DRUGS: MAST CELL STABILIZERS AND ANTIHISTAMINES

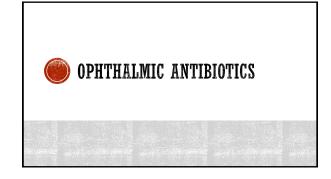


#### MAST CELL STABILIZERS, ANTIHISTAMINES

- Human eye has approximately 50 million mast cells containing granules containing chemical mediators
- Immediate hypersensitivity reaction triggered when antigens combine with IgE on the surface of mast cells
- Mast cells release histamine and other factors
- Histamine increases capillary dilation, conjunctival swelling and injection
- Safer than steroids for chronic use

#### MAST CELL STABILIZERS, ANTIHISTAMINES

- H1 antagonist: emedastine (Emadine), azelastine (Optivar)
- Mast cell stabilizers: cromyln (Crolom), lodoxamide (Alomide), pemirolast (Alamast), nedocromil (Alocril) take days to weeks to reach peak efficacy
- Mixed H1 antagonists/mast cell stabilizers: olopatadine (Patanol), ketotifen (Zaditor, Alaway), epinastine (Elestat), azelastine (Optivar)



#### OPHTHALMIC ANTIBACTERIALS



## OPHTHALMIC ANTIBIOTICS FLUOROQUNINOLONES

- •Fluoroquinolones:
  - ofloxacin, levofloxacin, ciprofloxacin, moxifloxacin, gatifloxacin, besifloxacin
  - Broad spectrum: gram-positive and gram-negative
  - Older generation have good potency with gram-negative
- Newer meds have expanding gram-positive coverage
- Treat corneal ulcers, conjunctivitis
- High rate of intraocular penetration

#### OPHTHALMIC ANTIBIOTICS SULFA DRUGS

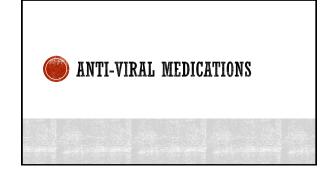
- Sulfonamides: sulfacetamide ophthalmic solution and ointment
- Sensitivity reactions 5% incidence
- More effective when combined with trimethoprim or pyrimethamine
- Cross allergenicity with non-antibiotic sulfonamides is unlikely based on chemical differences but is theoretically possible
- No cross-allergenicity between sulfonamide and sulfates

#### OPHTHALMIC ANTIBIOTICS AMINOGLYCOSIDE; IODINE

- Aminoglycosides: gentamicin, tobramycin
- Neomycin 8 % of patients (maxitrol) develop allergy
- Erythromycin, clarithromycin, azithromycin
- Bacitracin alone or in combination with polymixin, neomycin
- Polymyxin/trimethaprim (Polytrim) may be used sulfa allergic patients
- · Iodine:
- Topical povidone-iodine 5% solution: prepare surgical field and is important in prophylaxis against endophthalmitis
- Povidine iodine scrub damages corneal epithelium
- Iodine allergic patients do not use. Allergic to contrast media or seafood allergic probably OK to use

## COMBINATION ANTI-INFLAMMATORY, ANTIBIOTIC DRUGS





#### ANTIVIRAL DRUGS



### ANTIVIRAL DRUGS TOPICAL

- •Trifluridine (Viroptic) herpes simplex keratitis
- •Acyclovir 3 % ointment not available in US. 5% dermatological ointment not approved for ophthalmic use
- Ganciclovir gel 0.15% (Zirgan) approved for treatment of HSV keratitis

#### ANTIVIRAL DRUGS SYSTEMIC

- •Acyclovir (Zovirax) used to treat ocular HSV and HZV; 400mg twice daily prevents recurrence of epithelial and stromal keratitis
- •Valacyclovir (Valtrex) HZV but not HSV infections
- Famciclovir (Famvir) HZV reduces duration of post herpetic neuralgia
- Ganciclovir CMV retinitis intravitreal insert release drug over 5-8 month period