Miotics, Glaucoma Meds, Antibiotics, Corticosteroids, NSAIDS Antivirals, Antihistamines
Christopher J. McDevitt, M.D.

- Direct agonists
- Indirect agonist
- Antagonist

- Direct agonist:
  - Miosis, accommodation
  - Increase aqueous outflow, decrease IOP

- Acetylcholine 1% carbachol 0.01% intracameral use constrict pupil anterior segment surgery

- 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 COLUMBINE 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, acute angle 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

MYDRIATICS AND CYCLOPLEGICS

**Edrophonium test:** increases acetylcholine at neuromuscular junction

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**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
Norepinephrine (NE) is a transmitter.

- Alpha and beta receptors for NE
- Direct agonist
- Indirect agonist
- Antagonist

**Alpha-Adrenergic Drugs**

- Alpha-1 phenylephrine: Mydriasis stimulates iris dilator muscle
- Naphazoline: decongestant with reduced vasoconstriction and hyperemia
- Elevate systemic blood pressure
- Caution: using 10% phenylephrine topically; 5mg per drop, use with caution
- Systemic "pressor" dose bolus IV 50-100µg

**Alpha-2 Adrenergic Agonists**

- Apraclonidine (Iopidine): Pre and post YAG cap and SLT, cataract extraction to manage increased IOP
- Prevents NE release decreases 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

**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 80%
- Inhibit the normal physiological responses of increasing pulse and BP with exertion: may be poorly tolerated in active or elderly with routine activities
- Reduce brachyopasm in asthma and COPD patients
- 6 drugs:
  - Betaxolol selective β-1 inhibitor; 0.5% solution or 0.25% suspension (Betoptic S) less irritating
  - Nonselective β blockers:
    - Carbetolol (Ocupress)
    - Levobunolol (Betagan)
    - Metipranolol (Optipranolol)
    - Timolol maleate (Timoprol)
    - Timolol hemihydrate (Betimol)

**BETA-ADRENERGIC ANTAGONISTS**

| BETA-ADRENERGIC ANTAGONISTS || 
|---|---|---|
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| Levobunolol | Carbetolol (Ocupress) | 
| Metipranolol | Levobunolol (Betagan) | 
| Timolol maleate | Metipranolol (Optipranolol) | 
| Timolol hemihydrate | Timolol (Betimol) | 

**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 INHIBITORS**
- Systemic:
  - 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

**CARBONIC ANHYDRASE AND AQUEOUS HUMOR SECRETION**
- Topical:
  - Dorzolamide (Trusopt); In combination with Timolol (Cosopt)
  - Brinzolamide (Azopt)
**Prostaglandin Analogues**

- Latanoprost (Xalatan)
- Bimatoprost (Lumigan)
- Travoprost (Travatan)
- Tafluprost (Zioptan)
- Unoprostone (Rescula)

**Side Effects:**
- Ocular side effects: darkening of iris and periocular skin
- Hypertrichosis of eyelashes
- Cystoid macular edema (CME)
- Conjunctival hyperemia
- Uveitis
- Reactivation of HSV keratitis
- Use with caution in pregnant patients since uterine contractions are mediated by prostaglandins

**Routes of Administration**
- Local injection
- Ocular implantation
- Topical
- Systemically

**Categories**
- Glucocorticoids
- Non-steroidal anti-inflammatory drugs
- Mast cell stabilizers
- Antihistamines
- Antifibrotics

**Antifibrotics**
- 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
- Scleral melt
- Eyelid skin atrophy
**STERIODS 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
- Psychoses

**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)**
- Flurbiprofen 0.3% (Ocufen) first available topical NSAID used pre-op to reduce intraoperative miosis for cataract surgery
- Diclofenac 0.1% (Voltaren) prophylaxis and treatment of post-op inflammation and CME
- 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-ALLERGY MEDICATIONS**

**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:** cromylin (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 ANTIBIOTICS**

**OPHTHALMIC ANTIBACTERIALS**

**OPHTHALMIC ANTIBIOTICS FLUOROQUINOLONES**

- **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, clarihromycin, azithromycin
  - Bacitracin alone or in combination with polymyxin, neomycin
  - Polymyxin/trimethoprim (Polytrim) may be used sulfa allergic patients

- **Iodine:**
  - Topical povidone-iodine 5% solution: prepare surgical field and is important in prophylaxis against endophthalmitis
  - Topical povidone-iodine 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

ANTI-VIRAL MEDICATIONS

ANTIVIRAL DRUGS

Ganciclovir gel 0.15% (Zirgan) approved for treatment of HSV keratitis

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

Acyclovir (Zovirax) used to treat ocular HSV and HZV; 400mg twice daily prevents recurrence of epithelial and stromal keratitis