**OPHTHALMOLOGY**

**ANATOMY**

**Conjunctiva**
- Continuous membrane that provides nutritional support: tears, aqueous fluid
- Sections:
  - Palpebral conj: underneath the lid
  - Fornical conj: at the bulbopalpebral junction
  - Bulbar conj: directly on eye
- Creates the dead end: no, your contacts won’t be lost in the back of your eye

**Fovea**
- Highest concentration of cells
- Located at the center of the macula region
- Best visual acuity in this spot: responsible for sharp central vision (macular vision)
- Macular degeneration: 1 of 3 leading causes of blindness

**Cornea**
- Lots of innervation, even more than the brain (painful if poked!)
- If scratched, corneal epithelium can regenerate in 24 hr
- Scarring: cross links not organized anymore
- Layers: nonpolar epithelium (one layer), polar stroma, nonpolar endothelium → challenge for drugs to cross through

**BAB: blood aqueous barrier**
- Allows some of blood to get in
- Breaks down easily with inflammation → easier drug penetration
- Made up of iris blood vessels and ciliary body epithelium

**BRB: blood retinal barrier**
- Similar to BBB
- Difficult to get drug in (even with significant inflammation)
- Need to give drug intraocularly
- Made up of retinal pigment epithelium and capillaries

**DOSAGE FORMS**

**Ophthalmic drops**
- Volume of eye drops: 30-50mcl → eye can only hold 10mcl in tear film, waste the rest
- Absorption: 5 mins
  - Depends on tear turnover, pH, contact time
  - Therefore, 2nd drop is wasted if put in right after the first drop since it can’t be absorbed that quickly
- Techniques to aid absorption: punctual occlusion, eyelid closure (prevents systemic absorption)
- Corneal barriers preventing penetration: epithelium, stroma, endothelium (np→polar→np)

**Subconjunctival/SubTenon’s injections**
- Long acting steroids (e.g. triamcinolone, 3 months)
- For increased local concentrations, to avoid systemic toxicity
- Good for kids and noncompliant patients

**PATHOPHYSIOLOGY**

**Cataracts**
- Lens get opacified (cloudy)
- If you live long enough, everyone will get one eventually
- Leading cause of blindness in the world (not in the USA)
- Causes: trauma, disease states, drugs
- Sx: blurry, halo, bad night vision, slowly progressive changes
- Tx: surgical removal is common

**Glaucoma**
- 4 of 10 eye prescriptions are for glaucoma
- Chronic therapy needed (often 25+ years)
- Need multiple meds: 30% of patients
• Risk factors
  o ↑Intraocular pressure (IOP): most significant and the only manageable risk factor
    ▪ Normal pressure = 10-20mmHg
    ▪ Hypertensive = 22mmHg (w/o symptoms)
    ▪ Measured with a tonometer
    ▪ ↓Corneal thickness = ↑pressure
  o African Americans, Hispanics
  o Age, family history, overall health
• Two ways to manage it
  o Turn off aqueous fluid production in ciliary body
  o Open up drains: flow out of uveoscleral or trabecular outflow pathways
• Bath tub=ciliary body; drains=uveoscleral or trabecular outflow
• POAG: progressive open angle glaucoma → progressive optic neuropathy, damage to optic nerve, loss of retinal cells
• C/D ratio: cup to disc ratio
  o Used to measure progression of glaucoma
  o Optic disc = the eye’s blind spot where optic nerves and blood vessels enter retina
  o ↑Ratio = ↑loss of retinal ganglion cells
  o Retinal ganglion cells are support: when gone, the vasculature just hangs
  o Like a donut being eat from inside out (ratio of the donut hole to the donut grows)
• May eventually lead to tunnel vision: can only see right ahead of them, although vision can still be 20/20
• Best treatment method: ↓IOP
• 1mmHg = 10% ↓risk
• Note: glaucoma is not always associated with increase in pressure (e.g. normal tension glaucoma, more common in Asians)

Blephritis
• Inflammation of eyelid
• Causative bacteria: coagulase neg staph > staph aureus
• Chronic problem
• Tx: scrub with eyelid cleanser, warm compresses, artificial tears → if severe: erythromycin or bacitracin

Hordeolum
• Sty along the eyelid margin
• Focal infection
• Tx: warm compresses

Chalazion
• Cyst located higher up on the eye lid
• Inflammation, often chronic
• Tx: remove it

Conjunctivitis
• Inflammation of the conjunctiva (membrane lining eyelids)
  • aka “pink eye”
  • S&S: hyperemia (redness), burning, scratching, tearing, exudate (oozing), swelling, papillary hypertrophy
  • Usually no pain nor ↓visual acuity (pain suggests it has spread to the cornea, more serious)
• Causative organisms
  o If papillary conjunctivitis → cause is viral/bacterial
  o If follicular conjunctivitis → cause is viral
  o Viral
    ▪ Adenovirus is most common
    ▪ S&S: watery, no discharge
    ▪ Tx: gets the red out (↓hyperemia) but doesn’t get rid of bacteria; no antivirals
  o Bacterial
    ▪ Most common is staph aureus (for kids, H. influenza)
    ▪ S&S: mucous discharge, sticky, hyperemia
    ▪ Tx: almost everything works, wide spectrum antibiotics (best choice = TMP-polymyxin), sometimes systemic tx needed, quinolones are overkill
  o Allergic
    ▪ S&S: swollen lids, itchiness, no change in visual acuity
    ▪ 5 types total, the 2 most common:
      • SAC: seasonal allergic conjunctivitis → pollen, fall/spring; affects pts 20-40 y/o
PAC: perennial allergic conjunctivitis \( \rightarrow \) pet/mold/mites, pollen; affects infants
- GPC: giant papillary conjunctivitis
  - Soft contact lens wearers
  - Tx: steroids, mast cell stabilizer, decongestants (use only short term)
- Chlamydial
  - Systemic treatment required: tetracycline, doxycycline, erythromycin
  - Add on topical: tetracycline, sulfa, erythromycin (qid for 6 weeks)
- Usually no need to culture & stain, but yes for the following populations: neonates, kids with possible H. influenzae, pts with hyperacute conjunctivitis (which needs systemic treatment)
- Need gram stain/culture if purulent (pus), membranous, pseudomembranous
- Tx: usually self-limiting, goes away in a week or two
  - Tx available to shorten course of disease, reduce discomfort, stop spread

**Keratitis**
- Infection of the cornea (corneal ulcer)
- Affects visual acuity: big concern
- Types
  - Viral: most common type, HSV, with steroid/antibiotic use
  - Bacterial: gram + and gram -
  - Fungal: not too common, seen in agricultural/dirty injuries
  - Parasitic (acanthamoeba): cystic form lives in hot tubs, doesn’t go away quickly
- S&S: tearing, pain, hyperemia, photophobia, edema, hypopyon (collection of WBCs), iritis
- Associated with topical steroids, overnight wear of contact lens, trauma
- Risk factors: diabetes mellitus, rheumatoid arthritis, alcohol, immunosuppressants, dementia, cocaine

**Cellulitis**
- Preseptal cellulitis and orbital cellulitis are two distinct diseases that share a few similar clinical signs and symptoms
  - Presetal cellulitis: infection of the eyelid and surrounding skin anterior to the orbital septum
    - More common than orbital cellulitis
    - Begins superficial to orbital septum
  - Orbital cellulitis: infection of the orbital tissues posterior to the orbital septum
    - Front and behind the globe \( \rightarrow \) optic nerve \( \rightarrow \) CNS \( \rightarrow \) meningitis
    - S&S: vision loss, meningitis, death, fever, IOP, bad ocular movement (\( \leftarrow \rightarrow \uparrow \downarrow \)), lid swelling, proptosis
    - Causes: trauma, sinusitis, polyps, dental extraction, immunosuppression, diabetes mellitus

**Endophthalmitis**
- Inflammation of the intraocular cavities (e.g. aqueous/vitreal humors)
- Bugs get into back of eye \( \rightarrow \) proliferate \( \rightarrow \) destroy retina
- S&S: ↓ retinal reflex, pain, hypopyon, ↓ visual acuity
- Two types:
  - Endogenous: chronic; results from spread of infection from distinct source (e.g. endocarditis)
  - Exogenous: acute; results from direct inoculation or trauma (e.g. from cataract surgery)

**PHARMACOLOGY**

**GLAUCOMA**
- Cholinergics: Pilocarpine (IsoptoCarpine)
  - Dosing: qid
  - ↓IOP: ₪₪₪₪
  - SE: miosis, eye/brow ache, accommodative spasm, cataract
- Epinephrine & Dipivefrin
  - Dosing: bid
  - ↓IOP: ₪
  - SE: ocular stinging/tearing, macular edema, conjunctival deposits, systemic SE (↑BP, ↑HR, etc.)
- Systemic CAIs: Acetazolamide (Diamox), Methazolamide (Neptazane)
  - Dosing: bid, tid, or qid
  - ↓IOP: ₪₪₪₪₪ (good for acute pressure rise)
  - SE: paresthesias (tingling sensation), GI problems, metallic taste, CNS depression, hypokalemia, acidosis
- Topical CAIs: Trusopt, Azopt
  - Dosing: tid (bid if adjunct)
  - ↓IOP: ₪₪₪₪ (not as effective as systemic CAIs)
  - SE: bitter taste, eye stinging, ocular allergy, no significant systemic effects

**Effectiveness:** prostaglandins > timolol > brimonidine
- First line: prostaglandin or \( \beta \) blocker (cheaper)
- Second line: \( \alpha_2 \) agonist or CAI (Combigan or Cosopt)
• Beta blockers: **Timolol** (Timoptic), **Levobunolol** (Betagan)
  o Dosing: qd/bid
  o ↓IOP: ₪₪₪₪₪₪
  o SE: both ocular & systemic
    ▪ Ocular: minor things like burning, stinging, etc.
    ▪ Systemic: exacerbate COPD/asthma, heart disease, CNS depression
  o If drug gets into nasolacrimal duct → absorbed systemically

• Combination: **Cosopt**
  o Timolol + dorzolamide (β-blocker + CAI)

• α2 agonist: **Brimonidine** (Alphagan)
  o MOA: ↓aqueous fluid production + ↑uveoscleral outflow
  o Dosing: bid or tid
  o Brimonidine>apraclonidine: 22-32x more effective
  o ↓IOP: ₪₪₪₪₪₪ (similar to timolol)
  o SE: both ocular & systemic
    ▪ Ocular: allergy, burning, stinging, lid edema, no mydriasis, no tachyphylaxis, no eyelid retraction
    ▪ Systemic: dry mouth, fatigue, headache

• Combination: **Combigan**
  o Timolol + brimonidine (β-blocker + α2 agonist)
  o ↓IOP: ₪₪₪₪₪₪ (greater efficacy than the individual drugs alone)
  o Great: well tolerated, may improve compliance
  o Dosing: max tid

• Prostaglandin/prostamide: **Latanoprost** (Xalatan), **Travoprost** (Travatan), **Bimatoprost** (Lumigan)
  o MOA: ↑uveoscleral outflow + trabecular meshwork outflow (open up the drain)
  o Dosing: qd
  o ↓IOP: ₪₪₪₪₪₪ (best, most potent)
    ▪ Lowest IOP, only once a day
    ▪ Best diurnal control
    ▪ Best persistency data
    ▪ Bimatoprost is the most potent
  o SE: both ocular & systemic
    ▪ Ocular: hyperemia, iris discoloration, more pigmentation around eyelid, eyelash thickener, CME, iritis
    ▪ Systemic: minimal like upper respiratory infection, muscle/joint pain

**ALLERGIC CONJUNCTIVITIS**

• Mast cell stabilizers (MCS)
  o Nedocromil (Alocril)
  o For prophylaxis and acute treatment of allergic conjunctivitis
  o Dosing: bid
  o Immediate onset

• Anithistamines with MCS activity
  o Olopatadine (Pantanol, PataDay)
    ▪ Safe & effective (even for kids 2-3 y/o)
    ▪ Pataday dosing: qd
    ▪ Best activity for allergic conjunctivitis
  o Ketotifen (Zaditor)
    ▪ OTC
    ▪ Dosing: q8-12

• Steroids
  o Works well, but side effect profile doesn’t allow long term use
  o Short term use as a little boost when needed
  o Loteprednol etabonate (Alrex)
    ▪ Only steroid approved for this indication
    ▪ Soft steroid for allergic conjunctivitis
    ▪ SE: secondary infection, glaucoma, cataract formation

**KERATITIS**

• Viral
  o Trifluridine drops (Viroptic)
  o Vidarabine (Vira-A): only compounded by pharmacists
Ganciclovir gel (Zirgan)

Steroids: used in stromal keratitis (pinpoint lesions on cornea)

• Bacterial
  o Shotgun approach: alternate aminoglycosides and cefazolin (need very aggressive tx for mean bugs)
    • Soak eyeball in antibiotics: gent → cef → gent → cef → etc.
  o Fluoroquinolones: big kids on the block
    • Ofloxacin, ciprofloxacin, levofloxacin, gatifloxacin, moxifloxacin
    • Dosing: q30mins → around the clock!
    • SE: toxic to epithelium, slow healing, problem w/pt compliance
    • 4th generation: best!
      • Gatifloxacin (Zymar)
      • Moxifloxacin (Vigamox)
        o Better spectrum of activity
        o Better MIC (min inhibitory conc.) activity
        o Better pharmacokinetic properties
        o More $$$ but more aggressive
        o Less resistance: inhibit DNA gyrase and topoisomerase IV
        o SE: minor stinging/burning (from low pKa)

• Fungal
  o Natamycin (available only if special ordered)
  o Acanthamoeba (parasitic)
    • Neomycin, propamidine, PHMB (pool disinfectant), miconazole, clotrimazole
    • Difficult to treat, need combo products and quick follow up or else bad

CELLULITIS

• Preseptal cellulitis: oral antibiotics: augmentin, cefuroxime, dicloxacillin
• Orbital cellulitis: IV ceftriazone, nafcillin

ENDOPHTHALMITIS

• Intravitreal: vancomycin 1mg + ceftazidime 2mg
• Amikacin 200-400mcg
• IV or oral antibiotics
• Topical (as per keratitis)
• Vitrectomy: drain the abscess, suck out the bugs

CYCLOPLEGICS/ANTICHOLINERGICS

• Relaxation of sphincter muscle (dilation/mydriasis), paralysis of ciliary muscle (blurry vision)
• Anti-inflammatory action
• Caution in primary open angle glaucoma (POAG): may raise IOP
• Atropine: longest acting, allergic reaction
• Scopolamine: 1 week, CNS SE
• Homatropine: few days, weaker
• Cyclopentolate: most potent after atropine
• Tropicamide: weak, fastest agent
• Treats: iritis, hyphema (bleeding in anterior of eye), or for dilation/cycloplegia in an eye exam
• SE: blurry vision, photosensitivity, narrow angle glaucoma attack (in kids: rash, fever, irritable)

SYMPATHOMIMETICS

• Topical phenylephrine
• Direct α-1 agonist
• Ocular SE: stinging, rebound miosis
• Systemic SE (if multiple drops): tachycardia, ↑bp, stroke, MI, drug interactions
• Cyclomydril: for infants, combination product cyclophenylate + phenylephrine

α-BLOCKER

• Dapiprazole (RevEyes): reverses phenylephrine mydriasis
• Thymoxamine: reverse PE dilation(not available in US)