Glaucoma and Ocular Surface Disease

1. Comorbidity
    a. OSD
        i. Present in ~15% of those 65 & up; Much more common in persons w/ glaucoma
        ii. Up to 60% of glaucoma patients have OSD
    b. Glaucoma
        i. Irreversible optic neuropathy
        ii. Expected to be 80M worldwide in 2020
        iii. IOP is only modifiable risk factor
        iv. Up to 40% of persons with glaucoma require more than one IOP lowering agent in the US
2. Parallels in Glaucoma and OSD
    a. Chronic diseases
    b. Often mismatch of signs and symptoms
    c. Assessments of each can vary from doctor to doctor
    d. Diagnostic tests often variable and not conclusive of disease and/or progression
    e. Vision can be affected by both and both can affect quality of life
    f. Treatment can be complex with many treatment options available and variable on effectiveness
    g. Both require at home care on part of the patient (compliance) to be effectively managed
    h. Neither have a cure
3. Ocular Surface Disease
    a. Review normal tear film anatomy
    b. Review DEWS II
        i. Review new definition of dry eye
        ii. Figure to show how to diagnosis/test for dry eye
        iii. Table from DEWS that outlines the treatment based on severity
    c. Managing dry eye in the glaucoma patient
        i. Remember dry eye is multifactorial, look for all contributing factors, especially modifiable treatments or activities
            1. Past eye surgeries (esp glc, high blebs may make patients poor candidate for in office dry eye treatments ie mibo/lipiflow, but MG probing or tear care may be beneficial)
            2. Review oral medications; (list offenders) some may be modifiable *allergy meds*
            3. Systemic disease/medications- use of CPAP (encourage well fit mask and adequate lubrication and/or goggles) Parkinsons (decreased blink rate, stress increase lubrication)
            4. Environment- device use, fans, heat in winter; discuss use of moisture chamber goggles, no ceiling fan use, humidifiers
            5. Gender and age; decreased tear quantity and quality with increased age; hormonal contribution
            6. Look closely at the lid margins
                a. Identify rosacea and treat it

b. MGD- very prominent in glc patients esp on PGA
    i. Treat MGD: w/c's and in office tx's (micro-blepharoexfoliation/ thermopulsation)
c. Mechanical issues
    i. Incomplete blinking
    ii. Lagophthalmos (nocturnal)
    iii. Conjunctivalchalasis
d. CL wear
    i. Avoid soft lenses and consider RGP/scleral design if CL needed

ii. Patient education
    1. Key to success of both dry eye and glaucoma management
    2. Neither can be cured
    3. OSD can affect compliance to topical glaucoma medications that burn→increased risk of progression of disease

iii. Treatment options for dry eye in the presence of glaucoma
    1. Pay close attention to the medications the patient is on and/or ones that you may be starting patients on
        a. Preservatives- A 1999 prospective epidemiological survey of over 4K patients concluded that signs and symptoms were less prevailing with non-preserved agents. Also, most reactions were reversible upon discontinuing preserved agents
            i. BAK
                1. Quaternary ammonium compound w/ hydrophilic and hydrophobic elements (highly hydrosoluble) which makes them cause bacterial cell death by interacting w/ lipid components in the cell membrane→instability and release of cell contents
                2. Effect against Gram + and Gram –
                3. Most common preservative in ophthalmic medications
                4. Used in both dry eye medications and glaucoma medications
            ii. Alternative preservatives
                1. Polyquaternium-1 (polyquad)
                    a. Found in a number of dry eye products (Systane line and sooth XP)
                    b. Found in travaprost 0.003% (Izba- found in CA)
                2. Oxidizing preservatives
                    a. Sodium perborate (GenAqua and Dequest)

i. Found in dry eye products (genteal and thera tears)

b. Stabililzed Oxychloro Complex (SOC) or Purite
   i. Found in alphagan P
   ii. Ocupure, very close to Purite and used in some multidose dry eye preps

c. Sofzia
   i. Found in Travatan Z

3. Potassium sorbate
   a. Xelpros

b. Consider allergy or chemical toxicity
   1. May be BAK allergy or allergy to the active medication
      a. PGAs- allergy rare, 1.5%
      b. B-blockers- contact dermatitis 11-13%
      c. Dorzolamide- 3% dermatitis & 4% conjunctivitis
      d. Brimonidine reported 9 & 11.5%

c. Dosing- less is more when OSD present
   i. Consider once daily dosing of glaucoma medications
   ii. Take advantage of combination medications

d. Preserved vs Non-preserved therapies
   i. Therapeutic options for PF formulations
      1. Timolol PF (Timoptic Ocudose)
      2. PF Dorzolamide/Timolol (PF Cosopt)
      3. PF Tafluprost (Zioptan)
      4. Imprimis Rx
         a. Multiple PF options for different agents, including multiple combo options
   ii. Table with BAK free and NP options
   iii. Downfall for NP options
      1. Cost and insurance coverage (5-10x)
      2. Waste from left over medication
      3. Compliance an issue with correct usage and disposal; Single use, but pt will reuse→ increase risk of infection

2. Identify and treat underlying inflammation
   a. Look at Rx options (Restasis, xiidra, cequa, Klarity C)
   b. Caution use of steroids in glaucoma patients
      i. But when needed, PF steroids can be useful; watch IOP if prescribing
      ii. Loteprednol better choice

        c. Ocular Rosacea
            i. Lid hygiene (Cliradex)
            ii. Oral doxycycline 50 mg, consider long term
            iii. In office tx's (micro blepharoexfoliation, IPL, Lipiflow)
    3. Punctal Occlusion
        a. Can benefit both from dry eye but also allows for less systemic absorption = less side effects; possibly improved efficacy?
        b. Temporary collagen vs permanent silicone vs cautery
        c. Only consider if inflammation resolved/controlled
        d. Keep allergy sufferers in mind; temp during non-allergy season may be a better option
    4. Amniotic membranes
        a. Dry w/ BCL
        b. Cryo-preserved *C/I'd in tub shunts*
        c. Amniotic fluid drops (regenereyes)
    5. Autologous Serum Drops- Vital tears or local options (Well Health)
    6. Tear stimulation via nasolacrimal nerve stimulation (True Tear)
4. Glaucoma
    a. Review aqueous humor production and drainage pathway
        i. Diagram of aqueous humor pathway
    b. Treatment
        i. 1mmHg IOP reduction decreases risk progression 10%
        ii. Drops are often first line therapy for glaucoma
            1. Issues with glaucoma medications
                a. Association between chronic topical PGA use with MGD
                    i. Prospective cross-sectional study showed that long term use of PGA is associated with obstructive MGD
                b. Cross-sectional case controlled study showed that patients with multiple glaucoma medications had more unstable tear films and more severe drop out of their MGs.
                c. Compliance
                    i. Non-compliance has been reported to be around 30%, with some as high as 80%
                    ii. One study showed that only 24.2% of newly diagnosed glaucoma patients were compliant with their medications for 2 years
                    iii. As we increase the number of glaucoma medications, compliance decreases
                d. New Topical Glaucoma medications and where they fall into dry eye
                    i. Xelpros
                        1. Softer preservative
        iii. Nonsurgical Glaucoma Procedures to decrease drop dependence
            1. SLT earlier or first line

a. Introduced in 1995 by Latina and Park, FDA approved 2001
    i. Uses 532 nm Q switched, frequency-doubled, Nd:YAG laser, delivers pulse duration 3ns
    ii. Targets melanin in the trabecular meshwork and increases aqueous flow through trabecular meshwork
    iii. Uses 80-100 times less energy than ALT, less destructive
    iv. Metanalysis shows 6.9-35.9% reduction IOP
    v. Success in diurnal IOP fluctuation reduction 50%
    vi. Studies show variability in length of effectiveness from 9-24months
    vii. Found to be safe and effective to repeat laser if successful first treatment wears off with similar results to initial treatment
b. Laser in Glaucoma and Ocular Hypertension Trial (LiGHT)
    i. Treatment naïve patients
    ii. Eye specific targets (OHTN <25mmHg and 20% reduction, Mild <21mmHg and 20% reduction, Mod <18mmHg and 30% reduction, Severe <15mmHg and 30% reduction)
    iii. SLT arm at target at more follow up appointments over 36 months than drop arm
    iv. SLT arm showed less progression, fewer cataract and trabeculectomy surgeries
    v. SLT more cost effective
    vi. SLT and medications found equivalent health-related quality of life (HRQL)
c. Garg et al. No difference between SLT and drops as initial therapy for 20% absolute drop in IOP
    i. 74.6% of eyes treated primarily with SLT reached drop free IOP control at 36 months (either 1 or 2 SLT treatments)

iv. Surgical Glaucoma Procedures to decrease drop dependence
1. Predicated on sparing conjunctival tissue and leaving ocular surface unaltered
2. Cataract Surgery
    a. 2-4mmHg, can last 5 years
    b. Increases facility of outflow following cataract extraction
        i. Felt to be improved trabecular function, not increased access of aqueous to trabecular meshwork
        ii. 3 hypothetical mechanisms
            1. Lens changes to outflow pathway
            2. Post -operative inflammation

3. Fluidics of the surgery-forcing high volume of fluid under pressure through system increases it's patency

3. MIGs
    a. Trabecular microbypass stents
        i. iStent
            1. First ab interno glaucoma implant
            2. Approved for mild-moderate open angle glaucoma
            3. FDA approval single implant only at time of cataract surgery
            4. Bypasses trabecular meshwork allowing aqueous to drain directly into Schlemm's Canal
            5. Two implants more efficacious than one (mean IOP reduction 6.03mmHg vs. 4.67mmHg) (1.2 medication reduction vs. 0.97)
            6. likely led to 2 Inject implants being approved
            7. Adverse events 22.8%
                a. IOP spike>stent blockage>malposition>hyphema>corneal event>formation PAS
        ii. iStent Inject
            1. 2 heparin coated titamium stents implanted ab interno
            2. FDA approval two implants at time of cataract surgery
            3. Approved for mild to mod open angle glaucoma
            4. IOP reduction 8.52mmHg
    b. Schlemm's canal scaffold
        i. Hydrus
            1. Nitinol (nickel-titanium alloy)
            2. Dilates Schlemm's canal 4-5x natural width and has holes to keep from blocking collector channels
            3. FDA approved 2018 at time of cataract surgery
            4. Approved for mild to mod open angle glaucoma
            5. COMPARE study
                a. 1 Hydrus vs. 2 iStents, standalone MIGS
                b. For all time points up to 12 months Hydrus had higher IOP drop (1.7 vs. 1.0 mmHg, not SS) and fewer medications (-1.6 vs. 1 med), higher number of patients able to remain medication free (46.6% vs. 24%)

6. Comparable outcomes to canaloplasty
7. HORIZON study showed increased IOP reduction and medication reduction at 24 months in cataract plus Hydrus vs. cataract alone (20% reduction in IOP in 77.3% vs. 57.8%) (7.6 vs. 5.3 mmHg reduction in IOP)
8. Adverse events include hyphema, malposition, corneal event, cyclodialysis, iridodialysis, formation PAS

c. Ab interno Trabeculotomy
    i. Trabectome
        1. FDA approved 2004
        2. Bipolar 550 kHz electrode with adjustable power to ablate 90-120 degrees
        3. 18-40% IOP reduction and 40% reduction in medications
        4. Adverse events similar to above
d. Ab interno Canaloplasty (ABiC)
    i. Approved for mild, mod, and severe glauocoma, with cataract surgery or standalone
    ii. Can treat 360 degrees of Schlemm's canal
    iii. >30% IOP reduction at 12 months
e. Goniotomy/Trabeculotomy (Kahook Dual Blade, Trabectome, OMNI)
    i. Approved for mild, mod, and severe glaucoma, with cataract surgery or standalone
    ii. Can perform synechiolysis at time of surgery
    iii. Kahook Dual Blade
        1. Removes strip of TM 3-4 clockhours
        2. 12 month data: 26.2% mean IOP reduction
        3. 50% reduction in medications
        4. Adverse events rare and self limited and include IOP spike, hyphema, corneal event, iridodialysis
    iv. Trabectome
        1. FDA approved 2004
        2. Bipolar 550 kHz electrode with adjustable power to ablate 90-120 degrees
        3. 18-40% IOP reduction and 40% reduction in medications
        4. Adverse events similar to above
f. Endoscopic cyclophotocoagulation (ECP)
    i. Endoscopic probe with up to 2.0W diode laser
    ii. Treatment of at least 270 degrees
    iii. Over 30% reduction in IOP

iv. Has been shown to be effective in refractory glaucomas that had failed prior filtration surgery
v. Adverse events IOP spike>cataract>hyphema>CME

c. Current Studies/emerging therapeutics
    i. iDose/injectable bimatoprost/bimatoprost ring/travaprost plugs etc
    ii. Gel forming drops
        1. Brimonidine in rabbit models, lasts 28 days
    iii. Bimatoprost Ring
        1. Phase II studies
        2. Releases over 6 months
        3. 20% IOP reduction
        4. Noninferior to timolol
        5. 89% retention of ring at 6 months
    iv. Punctal plugs
        1. OTX-TP
            a. PF travaprost
            b. Expands when hydrated and lasts 3 months
            c. Sits below punctum but contains fluorescein so can be visualized
            d. Phase II studies show 88% retention at 75 days and slightly inferior to timolol
        2. Evolute
            a. Latanaprost core
            b. Phase II studies show 20% reduction IOP and 92% retention at 3 months
    v. Subconjunctival implants
        1. Durasert
            a. Transparent polymer tube that elutes latanoprost over 12 months
            b. Phase I and II trials underway
    vi. Injectables
        1. Subconj, intravitreal, suprachoroidal
        2. Most involve prostaglandins
    vii. Intracameral implants
        1. Bimatoprost SR
            a. Phase I and II studies show similar efficacy to topical bimatoprost and 71% effects lasted 6 months
        2. Travaprost XR
            a. In phase II studies, showed noninferiority to timolol
            b. 25% IOP reduction at 11 months
        3. iDose travaprost implant
            a. Implantable titanium reservoir is secured in angle-this can be removed and replaced
            b. Phase II studies show noninferiority to timolol

i. 30% reduction from baseline IOP at 1 year
ii. 2 drug elution rates-18 and 36 months
iii. No hyperemia reported yet
iv. Currently in Phase III trials

viii. Intrascleral implants
1. Ophthalmic Micropump
a. Resembles the plate of a tube shunt
b. Contains a refillable reservoir and small computer
c. Connects to a valved intrascleral tube that delivers nanoliter doses of medication into the eye
d. Wirelessly chargeable and programmable
e. In preclinical studies at this time

d. Case studies to put topics together in a clinical picture