

# *Innovations in Eyecare & Medicine*

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**John A. McGreal Jr., O.D.**

**Missouri Eye Associates**

**McGreal Educational Institute**

*Excellence in Optometric Education*

# **John A. McGreal Jr., O.D.**

Missouri Eye Associates

11710 Old Ballas Road

St. Louis, MO 63141

1.314.569.2020

1.314.569.1596 (Fax)

[mcgrealjohn@gmail.com](mailto:mcgrealjohn@gmail.com)

# Financial disclosure

None

# Latanoprost 0.005%

- n Indicated for treatment of glaucoma and OHTN
- n Once daily
- n Established safety profile
- n Preservative free (No BAK)
- n Single dose container has 5 drops
  
- n Avail as iyuzeh (Thea)

# **Brimonidine 0.35% /Visiox Pharma**

- Patented TearAct delivery technology
- Slow, consistent sustained release for IOP control throughout the day
- 1<sup>st</sup> once-daily brimonidine
- Easier compliance
- Established safety profile
- Avail as Brimonidine

# Fixed Combo Dorzolamide-Tim

## TID Superior to, Safe as BID

- Journal Drug Assessment Pakravan 2021
- Prospective, interventional
- Cosopt BID decreased IOP by almost 28% from baseline, increasing dose to TID provided further reduction by 12% and delivered a 40% reduction from baseline
- Fixed combinations of drugs are attractive because more than 50% of glaucoma pts required more than one drop to control IOP, and there is a direct correlation between number of medications and adherence to therapy

# Sustained Drug Delivery for Glaucoma

## □ Non-invasive

- Ocular rings under eyelids
- Drug eluting punctal plugs

## □ Invasive

- Drug eluting implants
  - Durysta (Allergan)
  - Travapro XR (Aerie/Alcon)
  - iDoseTR travaprost implant (Glaukos)
  - Travaprost intracameral implant (OTX)

## □ Investigational

- Supraciliary implants, microneedles, intravitreal nanosponges

# Glaukos iStent Trabecular Bypass - Next

- iStent Inject – second iteration
  - 0.4mm single piece mushroom shaped titanium stent with fenestrations placed ab interno with preloaded inserter allowing multiple placements without leaving the eye
- iStent Supra – targets drainage through uveoscleral outflow
  - Advantage is larger surface area and negative pressure gradient
  - 4mm titanium stent placed into the supraciliary space
  - Results – lower IOP by 20% and reduction of at least 1 medication



# Schlemm Canal Scaffold Implant

- Hydrus / Invantis
  - Alone or in combination with cataract surgery
    - 1.5 mm incision
  - Mild-moderate glaucoma
  - 8 mm long device, flexible biocompatible nitinol
  - Enters canal, resides in canal, provides tension on inner wall
- Results in significant, durable decreases in IOP and medication use
  - Best results in combined surgery – 16.6mm/0.1 Rx @24m
  - Alone results – 18.6mm / 0.5 Rx @24m
    - 70% less use of medications

# Sustained Drug Delivery for Glaucoma

## □ iDose (Glaukos)

- 1.8x0.5mm titanium implant
- Steady release of travaprost into AC
- Scleral anchor into TM
- Duration – 12 months or longer
  - Intended to be removed, replaced
  - 33% decrease in IOP at 12 weeks, stable, sustained
  - No serious AE
- 93% remained controlled at 1 year (slow release)
- 81% used no IOP lowering medication at 1 year (slow release)
- SE- mild iritis 6%
- Offers continuous, drop-free experience

# Sustained Drug Delivery for Glaucoma

- IOL Haptic-based Drug Delivery System (SpyGlass Pharma /Aliso Viejo, CA)
  - Single piece hydrophylic acrylic IOL
  - 2 small drug eluting pads that slide onto haptics and set at haptic-optic junction, allows standard IOL injector with sub 2.4mm incision
  - Delivers bimatoprost into aqueous
  - Duration – 3 years
  - Study (outside US) – 45% IOP reduction, 100% <18mm IOP, 100% off topical Rx
    - Future potential for AMD and uveitis

# Cataract Surg May Decrease Risk AD

- JAMA Internal Medicine 2022 LeeC
- Prospective, longitudinal study cognitively normal Kaiser Permanente Washington from 1994 – 2018
- Cataract surgery decreased the risk of dementia by 30%, even after adjustments for extensive list of cofounders
- Magnitude of results is surprising given that there is no treatment or prevention reliably shown to decrease risk of dementia
- Do healthier patients go on to have cataract surgery ?

# Cataract Surg May Decrease Risk AD

- ❑ After surgery there is more and better visual stimuli which may stimulate the brain
- ❑ After visual improvement pts are better able to engage with the world, less depression, more socialization, drive at night, go for a walk etc
- ❑ Cognitive overload is when brain is not getting visual stimuli and spend lots of energy trying to understand poor signals
- ❑ Intrinsically-photosensitive retinal ganglion cells (IpRCG) known to involve circadian rhythms and cognition wakened by quality, blue color of light postop

# Light Adjustable IOLs - RxSight

- n 4 weeks post-operative UV protection required
- n Adjust refractive error at 3 weeks post-op, Uses 380nm exposure of digital light at slit lamp system (Light Delivery Device)
- n Adjust RK at 5 wks, hold off early YAG caps
- n Contraindicated in herpetic dz, high risk drugs, retinal sx
- n Results
  - UCVA 20/20 @6m twice as high as monofocal surgery
  - Half are 20/15 or better
  - Allows correction of up to 2D sphere and -0.75 to 2D cylinder
  - 91.8% w/in 0.5D of target (same as LASIK)

# Virtual Reality for Glaucoma Perimetry

- Virtual Vision Health VR VF
- Problems of current practice
  - Requires dark room
  - Requires dedicated staff to coach, patch, trial lens
  - Not portable
  - Expensive to purchase & maintain
  - Inefficient “log-jam”
  - Unpleasant for patient – neck issues, wheelchairs, COVID, patching, one eye tested, chinrests, time to relocate patient from exam room to testing room, trial lenses, fixation problems, etc

# Virtual Reality for Glaucoma Perimetry

- Virtual Vision Health VR VF
- Solutions for current practice problems
  - No dark room
  - No dedicated staff to coach, virtual assistant coaches
  - No patching, both eyes open, better results in pt w macular dz
  - Portable, anywhere, any position
  - Less expensive !!
  - Most efficient !! Techs can do other functions
  - Patient satisfaction is unreal – technology always wins!
  - Staff satisfaction is unreal
  - Fast, familiar, out-of-box set up with wi-fi
  - Bascon Palmer genesis



# Assesmt of Remote Training, at Home

## Testing & Variability of VR Perimetry

- Ophthal Glaucoma ChiaZ 2024
- Feasibility of Home VF testing after remote training
- Cross sectional
- Vivid Vision Perimetry – virtual reality perimetry
- Remote training is feasible, and subsequent testing did not require interactions with caregivers or staff. There was low test-retest variability. This may be a viable supplement to provide equivalent or complementary results to that of standard in-clinic assessment of visual function in glaucoma

# Dexamethasone insert 0.4mg

- Indicated in treatment of pain & inflammation following ocular surgery, new expanded indication is allergic conjunctivitis
- Physician-administered hydrogel matrix intracanalicular insert
- Alternative to conventional steroid therapy
- Tapered dose lasting 30 days
- Placed in office or operator
- Avail as Dextensa / Ocular Therpeutix

# Perfluorohexyloctane / B&L

- Approved for the treatment of the signs & symptoms of dry eye disease (DED)
- Ophthalmic solution
- Semi fluorinated alkane
- First and only Rx eye drop for DED that directly targets evaporation – the leading cause of DE
- Dose – qid, over 18yo
- SE – blurred vision, conj redness, less than any alternative drugs!!
- Available as - *Miebo*

# Canalicular Gel / NordicPharm

- Approved for the treatment of the signs & symptoms of dry eye disease (DED)
- 20mg/ml (0.6ml), sterile hyaluronic acid gel
- One disposable, prefilled syringe, one-size-fits-all
- Store at room temp, inject w 27g cannula/syringe
- Inject 0.2ml after priming the injector
- Durable for 6 months, avoids loss, irritation, infection
- Removal is irrigation
- CPT 68761, modifiers E1-4, \$147 unilateral / \$221 Bilat
- Available as - *Lacrifill*

# Dry Eye Drink / BruderHealthcare

- ❑ Specifically formulated powdered drink pack added to water to help hyperhydrate pts without deleterious effects of sugar
- ❑ Most pts do not adhere to prescribed volume of water
- ❑ Included tumeric, DHA, taurin & green tea, natural electrolytes and omega-3s
- ❑ PM version replaced B vitamins and green tea extracts w melatonin, chamomile extract and valerian root extract
- ❑ Allows water absorption to double and reduces inflammation

# Pulsed Azithromycin v PO Doxy in MGD

- ❑ JAMA Ophthl Mar 2023 Upaphong
- ❑ Mod-severe MGD is typically treated with 6 week course of oral doxycycline, limited by compliance with long treatment and SE
- ❑ Study compared 6 week long treatment of oral doxy vs oral azithromycin 1g dose once weekly for 3 weeks
- ❑ Equivalency of both treatments established at 6<sup>th</sup> week by MGD score and OSDI score
- ❑ Pts treated with azithromycin had fewer gastrointestinal side effects (4.4% v 15.9%)

# Use of Topical Anesthetics in Pts w CA

- Annals of Emergency Medicine Feb 2024
- Guidelines state: in adult ED pts with simple corneal abrasions it appears safe to prescribe a topical anesthetic (proparacaine, tetracaine, oxybuprocaine) for use up to every 30 minutes as needed during first 24 hrs after presentation as long as no more than 1.5-2ml total is dispensed and remainder is disgarded
- Article describes evidence in ophthalmology literature about topical anesthtic use for pain control in PRK
- Given evidentiary shortcomings and and known toxicity this practice is NOT warranted

# Clin Features & Trt Outcomes of Carb-resistant Pseudomonas Keratitis

- JAMA Ophthal TrubinF 2024
- N 6,210
- Retrospective Observational
- Multidrug resistance PA is a serious threat – FQ, aminoglycosides, cephalosporins reported as resistant
- PA is leading cause of bacterial keratitis worldwide
- Feb 2023 CDC in collaboration with FDA issued national alert warning clinicians of extensive drug resistance strains of PA



# Clin Features & Trt Outcomes of Carb-resistant Pseudomonas Keratitis

Highlights the concerning progression in resistance and virulence of *P. aeruginosa*, emphasizes need for alternative therapies like RB-PDAT that have broad coverage and no known antibiotic resistance

Rose Bengal photodynamic antimicrobial therapy – uses diagnostic ophthalmic dye activated w green light to generate antimicrobial oxygen free radicals that damage DNA and cytoplasmic membrane of bacteria

Calls attention to importance of culture & genetics-based methods of pathogen identification

# Lofilaner 0.25% / TarsusPharm

- Approved for demodex blepharitis – 1<sup>st</sup> ever for demodex
- 58% of adults visiting eye doctors have infestation
- Ophthalmic solution
- Favorable safety profiles – small number of hordeola, SPK
- Dose – BID x 6 weeks, not with CL (discoloration)
- Saturn 1 & 2 Trials demonstrated eradication of mites, collarette reduction, eyelid erythema reduction
- Far better than out of pocket less effective options like blephEx, IPL, tea tree oils
- Available as - *Xdemvy*

# Loteprednol 0.2% / Lupin

- Approved for allergic conjunctivitis
- Topical safe steroid
- Less increases in IOP
- Less side effects
- This is a generic !
- Avail as Alrex

# **Loteprednol 0.2% / Cyclosporin 0.1%**

- ❑ Combination of two safe FDA approved drugs for DED
- ❑ Preservative-free
- ❑ Topical, safe steroid to relieve inflammatory component
- ❑ Topical safe T-cell drug to specifically treat dry eye dz
- ❑ Allows immediate treatment for both presenting issues
- ❑ Allow for one bottle of medication, not two
- ❑ Easier compliance
- ❑ Cost savings (\$69 for 5ml)
- ❑ Offer Klarity-C (cyclosporin 0.1% 5.5ml for \$1 extra)
- ❑ Avail as Klarity-CL (Imprimus)

# Tropicamide & Phenylephrine

- Drug device with combination drugs onboard
- Optejet drug delivery system – delivers spray mist
- Proprietary tropicamide and phenylephrine combination
- For in-office mydriasis
- Easier, faster
- Established safety profile
- Lower levels of pro-inflammatory cytokines
- Avail as MydCombi (Eyenovia)

# Geographic Atrophy - GA

- GA eyes lose 22 EDTRS letters over 5 yrs
- Median time to central GA in 1<sup>st</sup> eye after diagnosis is 2.5 yrs
- Median time to develop central GA in fellow eye is 7 yrs
- Development of or progression of GA over time is common cause of VA loss in eyes with nAMD
  - It is the final anatomic outcome leading to vision loss
- GA – degeneration of macular photoreceptors, RPE cells, choroid, thinning, atrophy, irreversible loss

# Geographic Atrophy - Background

- n Advanced progressive dry AMD
- n Irreversible loss RPE, photoreceptors, choriocapillaris
- n >5 mil worldwide, incidence similar to nAMD,
- n 1 mil US
- n Incidence quadruples q10yrs after age 50
- n 20% of all legal blindness
- n Under-diagnosed, prevalence increases as population ages

# Geographic Atrophy – Symptoms

- n Emotional, physical, social
- n Difficulty reading (100%)
- n Difficulty driving (75%)
- n Difficulty TV (69%)
- n Difficulty facial recognition (63%)
- n Our Goal should be to keep 20/100 or all is lost!



# Geographic Atrophy – Spectrum

- Early
- Intermediate
- Advanced
  - GA - 53.9%
    - Perifoveal disease can be 20/20
  - nGA - 47.6%
    - Characterized often by “Double layer” sign – little gap between BM

# Pegcetacoplan / Apellis Pharm

- Pegylated highly selective peptide
- Binds to C3, preventing its cleavage
- Inhibition of C3 prevents events in complement cascade (down-regulation)
  - Needed for opsonization, inflammation, formation of MAC that leads to cell death
- IVI – every month or every other month, safe
- Extrafoveal GA responds better, grows faster
- Decreases GA growth by 26%
- Avail as Syfovre

# Avacincaptad pegol / Iveric BIO

- Pegylated RNA aptamer
- Potent Specific Inhibition of C5
- Blocks cleavage of C5, therefore decreases MAC formation
- IVI – every month, safe
- Extrafoveal GA responds better, grows faster
- Decreases GA growth by 26%
- Approved August 4, 2023
- Avail as Izervay

# Benefits of Treatment of GA

- Treatment provides more subtle benefit by reducing the rate of progression of GA
- Treatment effects will be less immediate and easy to recognize, so the number of patients opting for IVI for GA likely to be less
- Every patient needs to be aware of the option and benefits, risks, alternatives – Optometry's major role
- Most Important – every eye care professional must screen for GA
  - Rate of progression is 0.5-2.5mm<sup>2</sup> / yr

# Artificial Intelligence Role in GA

- n Application of AI in screening & diagnosis of GA will be invaluable
- n AI algorithms will identify on color fundus photography, FAF, OCT the following:
  - Presence of lesion
  - Size of lesion
  - Location of lesion
  - Monitor for change over time or disease progression
  - Monitor for effects of drug treatments over time

# Doxycycline / Galderma for GA

- n Low dose TCN has many beneficial properties
  - Anti-inflammatory
  - Anti-oxidative
  - Protects RPE cells (oxidative)
  - Attenuates bright light photoreceptor damage
- n Phase 3 Trial underway
- n Avail as Oracea

# Future Applications in GA

- n Use of these drugs in patients with WET AMD
- n Use of these drugs in earlier stages of Dry AMD
- n Administering both anti-VEGF and Compliment inhibitors concomitantly
  - Remember GA is the final common pathway in advancing dry AMD and treated wet AMD
  - Certain to become a new standard for some patients

# Unanswered Questions

- n How to best identify at-risk patients developing GA before first eye loses VA?
- n How to re-educate patients that think there is no treatment for Dry AMD?
- n Will candidates with fairly normal vision be willing to undergo monthly intravitreal injections?
- n How will the usual issues around availability of family for transportation, insurance issues, out of pocket costs be barriers to entry or durability of treatments?



# Pentosan Polysulfate Sodium (Elmiron)

- n Approved for chronic interstitial cystitis in 1997
- n 2018 reported to be linked to vision threatening macular disease
- n Characteristic RPE atrophy resembles dry AMD
- n Continues to evolve after drug cessation for at least 10 years
- n Progressive RPW atrophy encroaches on foveal center poses risk of long term threat to central vision
- n OCT, FAF, IVFA and clinical examination are needed

# Aflibercept 8mg / Regeneron

- Approved for wet AMD
- Injection, intravitreal
- Fewer injections, long lasting control
- First and only anti-VEGF drug approved for immediate dosing at q8W and up to q16W intervals following 3 initial monthly doses (Pulsar Study)
- Fewer mean number of injections – 5.2 for EYLEA HD q16W and 6.1 for EYLEA HD q12W vs 6.9 for EYLEA 2mg
- Avail as EYLEA HD

# Faricimab 6mg / Genentech/Hoffman

- Approved for wet AMD & DME
- Injection, intravitreal
- Fewer injections, long lasting control
- Anti-VEGF humanized monoclonal antib with bispecificity to VEGF-A & Ang-2
- Fewer mean number of injections – from 1-4 months after initial once monthly loading dose for 4 months
- Often benefits “switch” patients (suboptimal responders or those with persistent intraretinal or subretinal fluid)
- Avail as Vabysmo

# Outcomes of Faricimab in Prev Trt AMD

- Ophthal Retina Pandit 2024
- N 218, 79.9 y, mean number of previous IVI before faricimab was 34.2
- Retrospective interventional review after 4 IVI of faricimab
- Faricimab improves anatomic outcomes and maintains vision. The proportion of eyes w sub retinal fluid was 53.2% before switching and and decreased to 26.6% after switching

# Intravitreal Injection Considerations

- Most common surgical procedure in US by eye MDs
- Endophthalmitis rate is 1/2500 injections (half cat sx)
- Typical pt is 81, female, w av VA of 20/80
- 8 million IVI/ year, 4000 of 18500 eyeMDs performing
- Reimbursement is \$120, rebate from manufacturers  
increase reimbursements significantly
- Avastin = \$70
- Lucentis = \$1575
- Eylea = \$1418, Eylea HD = \$2774
- Beovu = \$1997

# Home OCT for New Diagnosed nAMD

- Ophthal Retina BlinderK 2024
- Feasibility of daily Home OCT testing for nAMD
- Prospective, observational
- Notal Vision Home OCT demonstrated excellent frequency, quality, and accuracy of fluid detection. Pts found it easy and improved with experience. Better Wi-Fi and travel accommodations would allow for improved uptake

# At-Home OCT Device / Notal

- AI software evaluates biomarkers of nAMD remotely
- Obtains spectral-domain OCT images in a 10x10 degree area centered on fixation, then segments and estimates the volume of hyporeflective spaces
- Built-in wireless connection and data storage in Notal Health Cloud for analysis
- Two pivotal trials completed
- Adherence - 5.9 scans /wk, taking 48 sec to self-image
- Pt needs to enroll in “Scanly Home OCT Monitoring Program”
- Avail as Scanly

# Tyrosine Kinase Inhibitors

- Small molecules capable of diffusing into cells and inhibiting all VEGF isoforms as well as tyrosine kinase receptors
- Many are bioresorbables, sustained delivery lasting 9-12 months with single implant injected via pars plana 25 g needle or suprachoroidal administration, others are oral or sub-q, and 51% need no rescue medication, 79% reduction in treatment burden
- Bottom line – highly encouraging results for TKI in both AMD and DME, alleviates obstacles in current therapies



# PORT Delivery System / Genentech

- 1<sup>st</sup> Only continuous delivery system for nAMD
- Ranibizumab 100mg/ml – 6 month duration
  - 98% did not need supplemental therapy
- Approved for pts previously responding to 2 IVI of VEGF inhibitors, trials for DR and DME
- AE - conj heme, iritis, pain, endophthalmitis (2%) which is 3-fold higher risk compared to monthly IVI), decreased VA over 1<sup>st</sup> two months
- Patient selection, surgical techniques MOST important
- Avail as Susvimo

# PORT Delivery System / Genentech

- Voluntary recall in October 2022
- Septum of the implant was not holding and dropped into the tip preventing refill
- Attempts to refill required more pressure, and dislodgement of entire implant into the vitreous occurred – redesigned septum (double glued), more lubrication of refill needle, allow a safer device to be FDA cleared and available in October 2024
- Patients w original implant will need to have it exchanged
- Long lasting options are a HUGE benefit to all

# Ultra-Rapid Cooling Device / iRenix Med

- n Innovative approach to anesthesia for IVI
- n Rapid anesthesia in 10-20 seconds
- n Comparable to topical lidocaine
- n Complete nerve conduction block between 0 degrees C and 8 degrees C
- n No damage with temperatures to -30degrees C x 30 sec
- n Portable, hand held
- n Battery operated
- n Clinical trials at University of Michigan

# Multispot Pattern Laser / Zeiss

- n 532nm (green) solid state laser
- n Single spots or pre-programmed multi-spot patterns
  - Patterns for BRVO, CRVO, PDR etc
- n Multi-spot patterns
  - far shorter durations of pulse
  - More comfort to patient
  - Less time consuming to provider
- n Avail as VISULAS

# Phentolamine Ophth Sol 0.75% / Viatriis

- ❑ Indicated in treatment of pharmacologically induced mydriasis produced by phenylephrine or tropicamide
- ❑ Non-selective alpha-1 & alpha-2 adrenergic antagonist
- ❑ Onset of action – 30 minutes, max effect in 60-90m
- ❑ Precautions in uveitis
- ❑ Remove CL and wait 10 minutes before reinserting
- ❑ SE – stinging, discomfort, burning, hyperemia, dysgesia
- ❑ Supplied -box w 6 pouches containing 5 single pt vials
- ❑ Avail as Ryzumvi

# Epinephrine 1mg

- FDA approved – anaphylaxis
- >30 kg children
- Option for those preferring needle-free
- Nasal spray – end of auto injectors?
- Easier to carry and conceal
- 32 mil US w allergies (food)
- 50 mil US anaphylaxis to food, insect venom, medication and latex
- Available as neffy / ARS Pharmaceuticals

# Respiratory Syncytial Virus (RSV)

- n Very contagious virus, in healthy children (75%)
- n Serious respiratory illness for infants
- n Leading cause of hospitalization in <12 mos
  - 16 times higher than flu
- n Symptoms
  - Running nose
  - Fever
  - Appetite lost
  - Wheezing
- n 60% infected during 1<sup>st</sup> year, 100% by 2<sup>nd</sup> birthday

# Nirsevimab-alip

- Long acting antibody prevents RSV lower respiratory tract disease (LRTD) in all infants in and through 1<sup>st</sup> RSV season (October-April, varies by region)
- Indicated in children up to 24 mos, timed w start of RSV season - Provides rapid protection, single dose
- Trials – (Medley, Melody) 78.4% decrease in medically attended RSV LRTD w hospitalization
  - Post trial efficacy is 86%
- SE – minor rash at 14 d post dose
- “Breakthrough therapy” – designation
- Available as Beyfortus



# Respiratory Syncytial Virus Vaccine

- 1<sup>st</sup> FDA approved vaccine for prevention of LRTD caused by RSV in people over 60 yo
- 82% effective preventing lung & lower respiratory airway infection
- 94% effective preventing lung & lower airway infection in over 60 yo with asthma, COPD, CHF, DM, liver and pulmonary disease
  - Provides rapid protection, single dose, 0.5ml IM
- SE – minor rash at injection site, cold symptoms
- Available as Arexvy

# Ategepant / Abbvie

- Indicated – prevention of migraine in adults
- Only once daily oral 60mg (10, 30, 60)
- MOA – Calcitonin gene-receptor antagonist (CGRP)
- Episodic (61%) w 50-100% reduction in MMD
- Chronic (54%) reclaiming of 1 wk of migraine free days
  - Study group had 19MMD, 83% pretreatment exposure, 15 acute medication use days, 2/3<sup>rd</sup> overused acute medications
- SE – nausea (4%), constipation, fatigue
- Nearest competitor Nurtec ODT - 4.3 fewer MMD
- Available as Qulipta

# Fecal Microbiota

- Fecal microbiota, live-jslm
  - Fecal matter transplant for Clostridia difficilli
  - Available as Reboyota / Ferring Pharm
- Fecal microbiota product
  - 1<sup>st</sup> Orally administered fecal product
    - Manufactured from human fecal matter (live bacteria)
  - Indicated for prevention of clostridia difficilli infection in adults following antibiotic treatment
  - 460,000 / yr, 25% recurrence rate
  - Dose – 4 caps qd x 3 D
  - Available as Vowst

# Zuranolone / Sage-Biogen

- Indicated – 1st oral treatment for Post Partum Depression
  - Mental health conditions leading cause of maternal mortality with PPD being most common
  - Life threatening serious condition
  - Under-reported
- MOA – neuroactive steroid GABA-A receptor modulator
- Rapid improvement in symptoms @ day 15 and as early as day 3, Sustained effect to day 45
- Dose – 50mg qd, x 14 days

# Zuranolone / Sage-Biogen

- Indicated – only after pregnancy
  - Zoloft, wellbutrin, effexor approved during pregnancy
- SE – no driving until >12 hrs, no etOH , inc risk of fall
- Warning – controlled substance, potential for abuse/depen
- Breast feeding risks unknown
  - it is present in breast milk
- Unknown effects with other drugs
- Unknown costs
- Available as - *Zurzuvate*

# Fezolinetant / Astellas

- Indicated – treatment of severe vaso-motor symptoms (VMS) of menopause
- MOA – neurokinin 3 receptor antagonist
- Non-hormonal
- Regulates neuronal activity in thermo-regulatory center
- Dose – oral 45mg qd
- SE – abdominal pain, diarrhea
- Available as – Veozah

# Naloxone Nasal Spray/ Harm Reduction

- Indicated – opioid overdose
- OTC !
- MOA – opioid antagonist
- Dose – 50mg qd, nasal spray, rapid action
- Available as - *Revive*

# SGLT2 Drugs for Type 2 DM

- n Major Breakthrough in DM care, preventing major cardiovascular events (MACE)
- n Use of any SGLT2 increase urinary glucose
- n Reduces all cause mortality by 49%
  - Decreased MI by 19%
  - Decreases stroke by 32%
- n ADA Guidelines recommend SGLT2 as 2<sup>nd</sup> line therapy for type 2 DM after metformin
  - Especially in patients with pre-existing CVD
- n Available as
  - Invokana (canagliflozin)
  - Jardiance (empagliflozin)
  - Farxiga (dapagliflozin)
  - Steglatro (ertugliflozin)



# Bexagliflozin / Theracos Bio

- Indicated – Adults with Diabetes type 2
  - MOA – SGLT-2 inhibitor
  - Dose – 20mg once daily (am)
  - Available as – *Brenzavvy*
- 
- Indicated – Cats with Diabetes !
  - MOA – SGLT-2 inhibitor
  - 1<sup>st</sup> oral treatment for cats with diabetes
  - Available as – *Bexacat*

# GLP-1 Analog Drugs for Type 2 DM

- Major Breakthrough in DM care
- Drives better BG levels
- Easy once weekly injections!
- Available as
  - Victoza (liraglutide)
  - Ozempic, Wygovy, Rybelsus (semaglutide)
  - Trulicity (dulaglutide)
- Combination GLP-1 & GIP
  - Mounjaro (tirzepatide)
- Warning – national anesthesia groups reporting alarming cases of aspiration in patients on GLP-1 drugs having deep sedation, general anesthesia

# GLP-1 Analog Drugs for Type 2 DM

- Major recent findings of the benefits of weight loss drugs
- Used daily or monthly for weight loss
- Cardiovascular risks reduced
- Many consider this the “Age of Obesity Treatment”
  - Some consider it a chronic disease and recommend long term Rx
- Others consider the adverse events to outweigh the benefits
  - Nausea, vomiting, diarrhea, constipation, stomach pain
  - 7% drop out rate in trials due to side effects
  - Serious SE – pancreatitis, gall bladder & kidney issues
  - Argue for short term use along with diet exercise patient education
- Availability of drug is an important issue!
  - DM patients have difficulties procuring medication they need, not want
- Cost – black-market drug, PBMs denials, exorbitantly high costs
- Loss of control by the medical community

# Tirzepatide / Lilly

- 1<sup>st</sup> Dual agonist – GIP & GLP-1 receptor agonist
- Type 2 DM only at this time
- Dramatic lowering of HA1C & weight
- Available as 5mg, 10mg, 15mg
- SE – nausea, vomiting, diarrhea
  
- TED – Avail as Mounjaro

# Tirzepatide (Mounjaro) / Lilly

## □ SURPASS trial

- 7 studies
- Compared to placebo, ozempic, and 2 long acting insulins
- Performed better than all comparison groups
- Av 2% decrease in HA1C for av of 6.0
- Av weight loss – 15 lbs without insulin, 23 lbs with insulin

## □ SURMONT trial – N = 2,539 overweight or obese

- Weight loss 22.5%
- 63% lost 20%
- Not yet approved for pts WITHOUT type 2 DM

# Tirzepatide / Lilly

- 1<sup>st</sup> Dual agonist – GIP & GLP-1 receptor agonist
- Adults (>18) w obesity or excess weight and related medical problems
- Dramatic lowering of HA1C & weight
- Available as 2.5mg, 5mg, 7.5mg, 10mg, 12.5mg, 15mg
- SE – nausea, vomiting, diarrhea, gall bladder disease, reflux, pancreatitis, Low BG, depression, vision changes, thyroid tumors, thyroid CA, caution in multiple endoc. neoplasia synd. (MENS2)
- Avail as Zepbound

# Tirzepatide / Lilly

- 72-week study with diet & exercise & once weekly injection
  - 5mg = 15% (34lbs)
  - 10mg = 19.5% (44lbs)
  - 15mg = 20.9% (48lbs)
  - 1-in-3 at 15mg lost 58lbs
- Approval is for weight loss
- Avail as Zepbound

# Semaglutide / NovoNorDisc

- GLP-1 receptor agonist
- Oral
- Type 2 DM only at this time
- Increases insulin release from pancreas
- Decreases sugar released from liver
- Slows release of food from stomach after eating
- Available as 7mg, 14mg
- SE – nausea, abdominal pain, diarrhea
- Avail as Rybelsus



# Fenofibrate Use & Risk of Progression to Vision-threatening DR

- JAMA Ophthal MeerE 2022
- N 150,000 >18 y w NPDR from 2002-2019
- ACCORD - Fenofibrate use reduced DR progression
- FIELD – reduction in laser therapy in PDR & DME
- Mechanism unclear, used for cholesterol lowering
- This study - Fenofibrate use assoc w decreased risk of PDR and VTDR
- Use has fallen since development of statins but fortuitous unexpected renewed use is exciting

# Teprotumumab / Horizon

- 1<sup>st</sup> FDA approved treatment for TED
- TED – autoimmune disease, progressive inflammation, damage to orbital & ocular tissues, expansion of retro-orbital fat and EOMs, Proptosis, diplopia, optic nerve compression, vision loss
- Mediated by upregulation of insulin-like growth factor receptor on orbital fibroblasts, best treatment avail
- Traditional treatments are radiotherapy, IV methylprednisolone 5g (cumulative dose - 12 weeks) & orbital decompression surgeries
- Avail as Tepezza

# Grave's Disease (GD)

- Common autoimmune disease affecting 1-3% adults
- Onset between 30-50 yrs
- More common in females, more severe in males >50 y
- Ophthalmic signs - 20-50%, usually w/in 2 years of dx
- 90% of TED pts have hyperthyroidism, 10% euthyroid
- 40% clinical signs before diagnosis

# TED – Pathogenesis

- MOA – excessive orbital fibroblast (OF) activity is primary mechanism in GD
- Fibroblast derived from mesenchymal stem cells in bone marrow
  - Structural maintenance & produce extracellular matrix proteins like collagen and glycosaminoglycans
  - Capable of activating the immune system T-cells and cytokine secretion
  - Distinct populations of OF in GD have been identified
  - Insulin-like growth factor-1 receptors (IGF-1R) on OF are important factor in pathogenesis

# TED – Natural History

- Two phases of disease
  - Active phase – initial inflammatory phase
    - Clinical signs & symptoms progress rapidly
  - Inactive phase – fibrotic
    - After 6-18 months quiescence begins but pts rarely return to baseline
- Two subtypes of disease
  - Type I – younger, whiter & quieter presentations, more fat deposition in orbit, less diplopia and ON
  - Type II – older, smokers, overt anterior segment inflammation, chemosis, eyelid edema, more muscle involvement, ON

# TED – Clinical Signs & Symptoms

- Dry eyes
- Pain, FBS
- Blurred vision
- Double vision
- Increased redness
- Fullness to eyelids
- Facial asymmetry
- Eyelid retraction
- Proptosis
- Optic nerve compression

# TED – Clinical Evaluations

- Upper eyelid retraction is hallmark sign
  - Caused by proptosis or levator or Mueller hypertrophy or inc sympathetic tone
  - Margin to reflex distance (MRD1, MRD2)
  - Superior scleral show measured at 12:00 limbus
    - >5mm
    - Aymmetry of >1
- Von Graefe's sign – superior lid lag on downgaze
- Sensorimotor exam – most commonly involved EOM is IR, followed by MR, SR, LR, and obliques

# TED – Clinical Evaluations

- Proptosis – displacement of globe anteriorly can be measured by exophthalmometry or imaging
- Hertel exophthalmometry is quick, easy, reliable
  - Asians – 16-18mm
  - Caucasians – 18-20mm
  - Black – 20-22mm
- Proptosis reduction is primary measure of treatment outcomes and should be measured each visit and at baseline
- Conjunctival inflammations, caruncle enlargement, swelling of muscle insertions, corneal ulcerations



# TED – Clinical Evaluations

- Optic nerve disease – 3-7% of TED have ON
- Result of inflammation, compression, ischemia
- Rarely seen without overt EOM enlargement
- MR volume measured by CT imaging is the best predictor of DON (dysthyroid optic neuropathy)
- Most compression occurs at the orbital apex so disc changes are subtle or absent
- Testing
  - Visual fields – altitudinal or arcuate or para-central

# TED – Clinical Evaluations

## □ Testing

- Color vision – 77% of DON have reduced color vision,
  - specifically tritan Blue-yellow
- RNFL – thickens in inflammation, thins in compression
- GCL – IPL may be more sensitive for ON
- Macular OCT – useful as choroidal thickness varies
- OCT-A – notes changes in retinal and choroidal blood flow
- MRI – better for soft tissue differentiation but non-contrast CT preferred due to cost, availability and rapid acquisition time
  - EOM belly enlargement, fat expansion are hallmark radiologic findings

# Teprotumumab / Tepezza (Amgen)

- 1<sup>st</sup> FDA approved treatment for GD
- Fully humanized monoclonal antibody
- >2mm reduction in proptosis – 83%
- Reduction in diplopia - 68%
- Inactivation of dz – 59%
- Durable in most - Non-responders benefit from 2<sup>nd</sup> trt
- Dose - IV 10mg/kg x 1, then 3 weeks apart at 20mg/kg x 7, total 8 treatments
- SE – muscle spasm, alopecia, hearing impairment, hyperglycemia

# Teprotumumab / Tepezza (Amgen)

- Impressive results in proptosis and diplopia improvmt
- Not a “magic wand” in every circumstance
- ON not included in the clinical trial
  - IVMP highly effective in this senario
- Reactivation occurs in some (15%)
  - Most do well with second treatment with tepromumab
  - No RCT to support second treatments
  - Insurance issues / prior authorizations / high cost
  - Option is to revert to older strategies

# Teprotumumab / Tepezza (Amgen)

- Glycemic trend in TED patients treated with Tepezza
  - Uncommon in normoglycemic pts before treatment (10%)
  - Most hyperglycemic events happen with baseline pre-diabetes or diabetes and can be controlled with medication
    - Similar trends in retreatment group
    - Returns to baseline after treatment
- Hearing impairment – assess before during and after tx
- IBD – may cause exacerbation of pre-existing IBD

# Teprotumumab / Tepezza - Pearls

- Treat early and aggressively
- Control hyperthyroidism or hypothyroidism
- Stop smoking
- Comanage with the team – endocrinologists, internal medicine, oculoplastic ophthalmology, ENT
- Perform extensive pre-treatment PE, labs, CT
- Monitor closely repeating testing often

# Chloroprocaine gel 3%

- Indicated for ocular surface anesthesia
- Rapid onset
- Established safety profile
- Sterile single use unit
- Duration – 21.5 minutes
- No supplemental anesthesia needed
- No AEs
- No pain
- J-code for reimbursement (J-2403)
- Avail as IHEEZO (Harrow)

# Repository Corticotropin inj 80U/ml

- Indicated in severe acute or chronic allergic and inflammatory processes like keratitis, dry eye, iritis, diffuse posterior uveitis and choroiditis, optic neuritis
- Indicated in immune-mediated and idiopathic conditions across a range of therapeutic areas – exacerbation of SLE, dermatomyositis, psoriatic arthritis, RA, JRA, ankylosing spondylitis, sarcoidosis, multiple sclerosis, infantile spasms < 2yr
- Dose twice weekly injections at home with autoinjector
- Avail as Acthar Gel / Mallinckrodt



# Repository Corticotropin inj 80U/ml

- Highly purified formulation of ACTH
- Sustained release - gelatin 16%
- Subq or IM injection, biweekly, at home
- FDA approved 1952
- MOA
  - Activates MCRs
  - Inhibition of pro-inflammatory T cells, cytokines, fibroblasts
  - Minimizes IL, CD4, IgG on B cells
- There are 4 MC receptors in the eye
  - MC1R, MC3R, MC4R, MC5R

# Best Candidates for Acthar Gel

- Resisters – Rebounders – Responders
- Resistant to previous multiple treatments, treatment failures in severe keratitis, uveitis, dry eye
- Rebound after treatment tapers or discontinuation
- Responders – those who experience high IOP with sustained steroid therapies
  - Uveitis, keratitis, dry eye, corneal transplants
- Contraindications – same as steroids
- After 2 doses free cortisol equivalent to 10mg pred
- After 5 doses equivalent to 8.8mg pred
  - 2.5mg and 1.3mg above endogenous range

# Luca 3 Chest Compression System

- Uninterrupted compressions & complete chest rebound are keys to improving flow of blood to vital organs and survival
- Light, portable, does not get tired
- Frees staff for other critical functions
- Field, transport or hospital
- 100 compressions per minute @ 2" depth
- 45-minute battery, 4 hr recharge
- 60% increase in blood flow compared to manual
- \$20,000.

# XpertXpress (Cepheid)

- Rapid PCR diagnostic test
- Detects, differentiates SARS-CoV-2, Flu A, Flu B, RSV
- Rapid sample-to-answer
- 3 gene targets for more reliable SARS-CoV-2
- 1 cartridge, 4 tests
  - Swab
  - Transfer to cartridge,
  - Insert into platform
- Efficient, easy, point of care

# Inferior Vena Cava Filters

- “IVC” filters— small metal devices
- Granted “breakthrough device”
- Prevents inferior vena cava thrombosis in at risk patients
  - Injury to deep veins in leg
  - Surgery decreasing mobility
  - Clotting disorders
  - Pregnancy
  - Obesity
  - Contraindication to blood thinners

# Inferior Vena Cava Filters

- Prevents intravena cava thrombosis
- Symptoms
  - Leg heaviness
  - Pain
  - Swelling
  - Cramping
- Traps large blood clots, prevents travel to heart & lungs
- Permanent or removable – trend towards removal
- CavaClear IVC Removal Laser Sheath – lasers scar tissue around embedded filter device (80-90% success)

# Left Atrial Appendage Closure Device

- ❑ Candidates – aFib not caused by problems with heart valves, especially in those avoiding blood thinners due to risk factors like HTN, history of stroke, active jobs or high risk of falls
- ❑ As effective at preventing blood clots as blood thinning medications
- ❑ Procedure take 1 hr, place device in left atrial appendage via catheter in groin
  - Minimally invasive, overnight stay
- ❑ Discontinue regular blood thinners at 6 weeks
- ❑ Risks – blot clots, infection, stroke, pericardial effusion

# Left Atrial Appendage Closure Device

- 300,000 patients – proven
- 99% implant success rate, 0.5% major adverse events
- Effective – 96.2% discontinued oral anticoagulants
  - Still protected but off blood thinners
  - Back to activities
- Cost - \$2,600 out of pocket in typical traditional Medicare
- Available as – Watchman FLX / Boston Scientific



# Obstructive Sleep Apnea and The Eye

- OSA affects 15-20 million in USA
- Ocular manifestations
  - Glaucoma, NAAION, keratoconus, AMD, Diabetic retinopathy
    - Strongest for diabetic retinopathy
- Non-ocular manifestations
  - HTN, stroke, MI, Afib, Diabetes
- WestSD Eye Disorders Associated with Obstructive Sleep Apnea Curr Opin Pulm Med. 2016; 22:595

# Inspire Upper Airway Stimulation

- “IUAS” – neurosensory device,
- 2 incision procedure, 80 minutes, 7-10 d recovery
- Selection criteria
  - Diagnosis moderate-severe OSA
  - Struggle w CPAP or no benefit
    - Apnea hypoxia index 15-65
  - Not significantly obese (BMI 32-35)
- Device
  - Implantable pulse generator (IPG)
  - Sensor
  - Stimulator lead around the hypoglossal nerve

# Inspire Upper Airway Stimulation

## n Procedure

- Implanted deep under skin of pectoral muscle
- Between 2<sup>nd</sup> & 3<sup>rd</sup> rib
- The generator and sensor are both implanted in the same location
- Compare to maxillomandibular advancement 87% effective

## n Results

- 90% of bed partners report no snoring
- 91% patient satisfaction
- 79% reduction in apnea events
- 94% better than CPAP

# Transcatheter Aortic Valve Replacement

- “TAVR” – minimally invasive heart surgery
- Indication – aortic valve stenosis ( between Left ventricle and aorta)
- Symptoms – chest pain, SOB, fatigue, fainting
- Access – femoral artery, carotid, transapical (chest) or vena cava (stomach)
- Benefit – minimally invasive, solution for patients not a candidate for “open” surgery

# Xanomeline and Trospium / BMS

- New FDA approval for treatment of schizophrenia
- 125mg/30mg, 120mg/20mg, 50mg/20mg
- First new medication for psychosis that does not act on dopamine
- Main benefit is far fewer side effects, esp wt gain
- Cost - \$22K, 2 other drug failures required
- AE - nausea, constipation, and rapid heartbeat
- Available as – Cobenfy

# Link Between Vaping & Ocular Cancer

- Indian J Ophthal 2020 Shields, CL
- Vapors from e-cigarettes chronic exposure causing severe respiratory disease
- Conjunctival intraepithelial neoplasia (CIN) diagnosed in young adults with chronic vapor exposure is a form of ocular surface squamous neoplasia (OSSN)
- Carcinogens blown out of mouth settle on mucous membranes of eyes
- Trend to more aggressive variant of OSSN that occurs in the inferior fornix rather than then limbus

# Increased Cancer in Young Adults

- Lancet Public Health Dahut July 2024
- American Cancer Society & Univ Calgary
- N 23 million pts w diagnosis of CA, 7 mil died
- Identified 17 cancers types more common in Generation X and Millennials than older age grp, and 5 with increased mortality
- Uterine Ca increased 169% if born in 90s vs 50s
- Causes could be early exposure to environmental factors, climate, diet, decreased physical activities, obesity, DM

# 17 Increased Cancers in Young Adults

- Gastric cardia
- Small intestine
- Estrogen receptor positive breast\*
- Ovary (12%)\*
- Liver & intrahepatic bile duct in females\*
- Non-HPV assoc oral & pharynx cancers in females
- Anus
- Colon and rectal
- Uterine corpus (169%)



# 17 Increased Cancers in Young Adults

- Gallbladder \*
- Kidney\*
- Pancreas\*
- Myeloma\*
- Non-cardia gastric
- Testes
- Leukemia
- Kaposi sarcoma
- 10 of 17 of these cancers increased incidence in cohorts related to obesity (\*)

# 17 Increased Cancers in Young Adults

- Since cancer requires time to develop, obesity related cancers in young adults could be assoc w childhood (teens) health
- Earlier screening is necessary and already happening
  - Breast screening at 40yrs every other year
  - Colon screening at 45yrs
- Good news – cancers related to tobacco like lung ca and HPV related cervical ca are declining

# Radiopharmacology

- n Delivery of radioactive drugs to cancer cells directly
- n Main focus for now is neuroendocrine tumors & prostate
- n >5B market for prostate and small cell lung alone
- n Manufacturing & delivering drug is not easy
  - Radioactive
  - Degrades quickly (within days)
  - Logistics are manageable
- n Good long term profits
  - Too hard to make generics
  - Too expensive to make generics

# Radiopharmacology – \$10B Investment

- Novartis – has 2 drugs
  - Pluvicto – radioligand therapeutic targets PSMA in ProstCA
    - IV q6w x 6
  - Lutathera – for rare type of pancreas Ca and GI tract (4B)
- Bayer – has 1 drug
  - Xofigo – resistant prostCa and those with metastasis
- Bristol Mayers Squib
- AstraZenica
- Pfizer
- Eli Lilly

# Alzheimer's Dementia (AD)

- JAMA Neurology July 2024
- Cognitive combination blood test for cognitive decline is 90% accurate in determining if memory loss is AD!
  - PCP diagnostic success – 61%
  - Neurology diagnostic success – 73%
- Plasma phosphorylated tau 217 – biomarker for early dz
- Blood amyloid-B 40/42 ratio test – inc diag accuracy of p-tau
- Findings confirmed with PET
- Newest drugs like lecanemab & donanemab target AB are less effective in pts with advanced tau pathology JAM

*Thank you*