# Ophthalmic Update 2019

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# Cataract Surgery and Corneal Topics

# Cataract Innovations

- Drop Free cataract surgery and eye drops to reduce cataracts:
  - Intracameral injection of antibiotic, either cefuroxime or moxifloxacin
  - Subconjunctival injection of triamcinolone.
  - Reducing cataracts with an eye drop:
    - Study of 2 families with congenital cataracts found gene mutation in lanosterol synthase gene (LSS)
    - Lanosterol is a naturally occurring steroid keeping the lens proteins from aggregation and forming cataracts.
    - In dogs cataracts reduced with lanosterol eye drops
    - Lanosterol is a large molecule and with nanoparticle technology increases cornel penetration of the lanosterol
    - VP1-001: eye drops used to stabile and improve lens clarity in mice.
- Refractive indexing: changing the refractive index ab interno for an IOL without measurably changing its shape
- Uses an ultrafast femtosecond laser with 100 times less pulse energy than commercial femtolasers
- Works well with commercially available hydrophilic and hydrophobic acrylic IOLs.
- Precise within 0.1 D of target
- Treat up to +/- 4 diopters
- Used to treat residual myopia, hyperopia astigmatism, higher order aberrations
- Create diffractive bifocal and trifocal effect in IOL
- Application : pediatric cataracts, residual refractive error after cataract surgery
- Convert monofocal iol to multifocal; pts not adapting to multifocal

# ROCK Inhibitors and Corneal Diseases

- DSAEK and DMEK advances in corneal endothelial transplantation
- New approach with injection of cultured endothelial cells ROCK inhibitor into 11 eyes with corneal decompensation
- ROCK inhibitor can increase the energy and increase endothelial viability and adhesion and increase endothelial cell proliferation
- Two years after injection 100% of eyes with improves corneal thickness and endothelial cell counts greater that 500 cells/mm SQ
- ROCK inhibitors can decrease corneal neovascularization
- Promote epithelial wound healing
- May be used to treat severe corneal edema after cataract surgery

# Povidone-Iodine (PI) and Cataract Surgery

- PI kills bacteria quickly at dilute concentrations (0.05%-1.0%)
- Toxicity is related to concentration
- Current recommendations are 5% PI before cataract surgery (3 min)
- Polyvinylpyrrolidone (PVP) referred to as “povidone” complexed with iodine =povidone iodine (PI)
- Reduces endophthalmitis rates from 0.24% to 0.06%

- PI:
  - Iodine is used as a complex of polyvinylpyrrolidone and iodine (PI) to increase water solubility and decrease irritant and allergic reactions
  - Antisepsis is attributed to wide spectrum of activity and limited instances of microbial resistance.
  - Affordable, available
  - Targets the cytoplasm with killing takes place in seconds

# Surgical Adhesives in Ophthalmology

- Synthetic glues cyanoacrylate and polyethylene glycol (PEG)
- Biologic glues (fibrin) 2 part mixture
- Surgical applications:
  - Pterygium surgery
  - Limbal stem cell transplantation
  - Glaucoma surgery
  - Refractive surgery (epithelial in growth
- Surgical applications
  - Corneal perforations and melts
  - Corneal transplants
  - Cataract surgery
  - Strabismus surgery (conjunctival wound closure)

# Role Phacoemulsification in Glaucoma Therapy

- Cataract surgery can decrease IOP
- Angle closure glaucoma (ACG): IO decrease -6.4mm HG
- Primary open angle glaucoma (POAG) -2.7m Hg
- Pseudoexfoliation (PXG) -5.8mm Hg
- Phaco emulsification  is also combined with minimally invasive glaucoma surgery (MIGS)
- Effect of pre-op IOP the higher the pre-op IOP the larger the drop in IOP with phacoemulsification.
- For each 1 mm pre-op IOP an additional 0.85 mm decrease occurred
- Durability: similar effects at 6 and 12 months

# Cataract Surgery and the Rate of Traffic Accidents

- Greater than 500,000 patients record reviewed
- A reduced rate of hospital visits due to a traffic crash when the cataract surgery patient was the driver
- 4680 traffic crashes occurred during the baseline interval
- 1200 traffic crashes took place during the follow up after cataract surgery
- Results suggest that improvement in vision following cataract surgery are associated with decreased driving risks
- Post surgery crash rates were highest in the first month after surgery
- May want to spend time counseling post surgery about the risk in the first month after the surgery

# Scleral Contact Lenses

- Large diameter rigid gas-permeable lenses
- Designed to rest on the sclera, vault over the entire cornea
- Can transform an irregular corneal surface into a smooth optical surface
- Space behind lens is a fluid reservoir
- Provide relief for ocular surface disease
- Indications: corneal irregularity, ocular surface disease and severe refractive error
- Drawback: costs and convenience
- Fitting: special training, time consuming
- Cost $500 per lens plus fitting fees
- Not covered by many insurance plans

# Scleral Contact lenses

- PROSE (Prosthetic Replacement Ocular Surface System) fitter customizes the design and shape
- Fitter uses computer-assisted design system
- PROSE $5000-$7000 per eye for entire process
- Lower cost option: commercially available lenses
- Fitter uses diagnostic lens set to determine the correct sagittal depth and overrefraction to obtain lens power.
- The back surface peripheral curve system can be modified to provide the beat fit
- Using the diagnostic lens set decreases the cost to $1000 to $5000 per eye
- Other options are small lenses: minimal scleral, semiscleral, corneoscleral
- An alternative to tarsorrhaphy, amniotic membrane or keratoplasty

# Accuracy of IOL Calculation Formulas

- Accuracy of Barrett Universal II, Haigis, Hoffer Q, Holliday 2, Olsen and SRK/T for the Alcon SN60WF and SN60AT
- WK adjustment caused an overcorrection of hyperopic outcomes in long eyes resulting in more myopic outcomes then planned.
- Figures 4 and 5

# Glaucoma

# Rho Kinase Inhibitors in Glaucoma Treatment

- Primary mechanism of action differs from other glaucoma meds
- Normalize outflow resistance
- Work on the cytoskeleton of the trabecular meshwork decreasing the density of actin stress fibers in TM and Schlemm's canal
- Lead to smooth muscle relaxation and conjunctival hyperemia
- Two Rho kinase inhibitors approved for glaucoma treatment: netarsudil (Rhopressa) and ripasudil
- Side effects are hyperemia and subconjunctival hemorrhages
- Blepharitis
- Corneal verticillate
- A large number of patients in clinical trials with drew because of adverse effects

# Effects of Intravitreal Injections on IOP

- Volume driven acute ocular hypertension immediately follows intravitreal injection
- Transient and well tolerated
- Chronic sustained elevation in IOP is associate with repeated intravitreal I
- Risk factors for chronic ocular hypertension injections: number of injections, greater frequency of injections, and preexisting glaucoma
- IOP rise to an average of 46 mm Hg then quickly (2-3 minutes) returns to normal
- Proposed mechanisms: microparticle obstruction toxic or inflammatory effects on the trabecular meshwork
- Alteration of outflow facility by anti VEGF agents
- Conjunctival reflux after injection decreases Risk of IOP rise
- Smaller vitreous volume in smaller eyes as a risk factor
- 50 microliters injected into average vitreous volume of 4.5 to 5.0 ml

# Effects of Anti-VEGF IVI on IOP

- Prophylaxis:
  - Apraclonidine: treated group with increase of 37.3 mmHg vs 46.4 mmHg none
  - Timolol gel 0.1% 2 hours before injection: average IOP 25.5mmHg vs 29.3 mmHg in control.
  - Dorzolamide-timolol: 14mmHg treated vs 28.2 mmHg control; similar effect as apraclonidine
  - Brimonidine-timolol treated 28.4 mmHg and control 34.1mmHg
- Brinzolamide-timolol treated 14.87 control 28.21 mmHg
- Studies using oral Diamox have not showed any significant prophylactic benefit
- Patents receiving more than 7 injections per year
- Ranibizumab more than aflibercept?

# Ocular hypertension treatment study (OHTS)

- Phase 1: determine age, higher IOP, thinner central corneal thickness , large C/D ratio and higher visual field PSD separate individuals into high and low risk to develop POAG.
- Phase 2: high risk patients when treated reduced 5 year incidence of POAG by 60%.
- No benefit of early treatment for low risk patients.
- African Americans develop POAG at a higher rate despite similar baseline IOP and treatment
- Delaying treatment until VF abnormalities occurred only had a modest impact on rate of VF loss
- It is still necessary to assess both structural and functional testing

# Neurophthalmology

# Management of Acute Retinal Ischemia

- Vascular transient monocular vision loss (TMVL), branch retinal (BRAO) central retinal artery occlusion (CRAO).
- Retinal ischemia is associated with higher risk of stroke and cardiovascular morbidity and mortality
- New guidelines emphasize the urgent brain MRI with diffusion weighted imaging, vascular imaging and clinical assessment
- Goal: Identify patients at risk
- Risk is highest for second event, after the retinal event, within the first few days after the onset of vison loss
- Important for eye professional to make rapid referral to stroke center for work up
- Only need to refer promptly if seen within a few days of the visual loss

# Optic Neuritis and Autoimmunity Phenotypes

- Two new glial autoantibodies have been discovered
- Lead to a better characterization of a subset of inflammatory demyelination including optic neuritis
- 1) **Aquaporin 4 IgG (AQP4-Ig)** is the pathogenic antibody causing neuromyelitis optica (NMO): optic neuritis and spinal cord demyelination
- 2) Antibodies to **myelin oligodendrocyte glycoprotein** (MOG) found in a subset of optic neuritis patients

# MOG and AQP4-Ig and Optic Neuritis Treatment Trial

- Sera from patients in Optic Neuritis Treatment Trial (ONTT) analyzed for MOG and AQP4-Ig.
- ONTT patients with optic neuritis only
- None had positive AQP4-Ig
- Three positive for MOG
- MOG positive patients had negative MRI and none developed MS
- MOG is a distinctive disease entity causing optic neuritis: patients more likely to have optic disc edema, recurrent optic neuritis and not have MS
- MOG and AQP4-Ig may be found less than previously found in other studies

# MOG and AQP4-Ig and Recurrent Optic Neuritis

- One third of recurrent optic neuritis (rON) were positive for MOG or AQP4-Ig
- MOG positive patients did not have MS like MRI lesions and MS did not develop
- Patients with positive AQP4-Ig had course of severe permanent visual loss.
- Positive MOG had more rON but responded well to treatment and maintained better vision
- rON patients AQP4-Ig and MOG are valuable biomarkers
- Positive MOG more associate with bilateral optic neuritis
- MOG positive have  MRI findings different than MS respond well to corticosteroid therapy
- Positive AQP4-IG with severe visual impairment

# Retinal Microvasculature and Preclinical Alzheimer Disease (AD)

- Preclinical AD can be diagnosed measuring amyloid burden in the CNS.
- Compounds that bind amyloid in CNS can estimate disease burden when viewed with positron emission tomography (PET)
- In addition spinal fluid levels amyloid and tau protein can be measured
- Preclinical AD is recognized as a period of key changes before patient develops symptoms
- Previous studies have identified venous thinning on color fundus photographs. In addition reduced blood flow found in AD and mild cognitive impairment (MCI)
- OCT Angiography (OCTA) suggested decreased density in deep vascular plexus
- Clinical trials underway to prevent neuronal loss in AD it is important to be able to identify with preclinical AD

# OCTA Findings with AD and MCI

- Using OCTA participants in the study with biomarker-positive findings for preclinical AD had retinal microvascular changes detectable with OCTA compared with control individuals with biomarker negative
- The foveal avascular zone was larger with preclinical AD ,biomarker positive
- Compared with out biomarker preclinical negative
- Foveal avascular zone enlargement may offer cost efficient, noninvasive rapid screen to identify preclinical AD

# Pediatric Ophthalmology

# Outdoor Activity and Myopia Progression in Children

- After 1 year children with at least 11 hours per week outdoors with exposure to light intensity of at least 1000 lux lad significantly less myopic shift and axial elongation than those in the control group
- Groups wore light meter recorders and parents completed weekly activity diaries
- Risk of rapid myopia progression was 54% lower in the intervention group
- Protective effect was seen among myopic and non-myopic children in the intervention group
- Authors conclude that exposure to strong sunlight may not be required for myopia prevention
- Longer periods of low outdoor light intensity as in shade trees may be sufficient for the protective effect

# Preschool Vision Screening

- Three studies have demonstrated the effectiveness of preschool screening in decreasing risk of amblyopia
- Reliable, validated devices are available
- Initially in nonmedical preschool environment but becoming more standard in primary care provider
- Present techniques : handheld devices that estimate refractive error, assess ocular alignment and potentially detect risk factors for amblyopia
- Screening of children ages 3-5 years
- The prevalence of refractive errors that potentially cause amblyopia is several times greater than the prevalence of amblyopia

- Photoscreening technology: OSS-C photoscreener, iScreen 3000 and GoCheckKids (uses smart phone technology
- All have adequate sensitivity, specificity and predictive value (75%, 88%, 89%)
- Autorefractor technology
- Monocular: Retinomax and SureSight
- Binocular: PlusoptiX SPOT and 2WIN
- Blinq Pediatric Vision Scanner uses retinal polarization scanning technology

# Amblyopia Therapy Medical Advances

- Binocular therapies: improve amblyopia with binocular stimulation
- Two mechanisms: perceptual learning and dichoptic training
- Perceptual learning “practice makes perfect”: single visual percept is administered to both eyes simultaneously
- Dichoptic treatment presents independent stimuli to each eye unlocking binocular visual function
- Dichoptic: image shown to amblyopic eye is of higher contrast than non-amblyopic eye
- Use red-green dichoptic images with red-green glasses and I pad display
- Problems with compliance as patient tires easily with the IPAD game and does not complete the required time for treatment; need for more engaging games
- Failed to demonstrate non-inferiority with standard treatment (patching)

# Amblyopia Medical Therapy

- Increased levels of dopamine may improve vision
- Medication is levodopa
- Several studies evaluating levodopa mostly older children: PEDIG:L dopa and 2 hours of patching found no significant change.
- Other study with full time patching and L dopa vs placebo and patching found visual gains in the L dopa group

- Citicoline  used for recovery nerve cell damage from trauma
- initial wok in adults with amblyopia alone and in addition to patching with

# Amblyopia Therapy Advances: Refractive Therapies

- Anisometropia differences in hyperopia (> than 1.5 D SE) and Astigmatism (>2D SE)
- Myopia <3D anisometropia usually does not cause amblyopia.
- Ametropia: less exact: hyperopia >4D, >2.5 D astigmatism or >6 D myopia place child at risk
- Options are contact lens wear and surgery
- Surgical options for those with non-compliance with spectacle wear or standard treatment non-responders
- Laser refractive surgery reports for high hyperopia, myopia and astigmatism
- Well tolerated having low rates of complications
- Regression occurs across all groups of preoperative refractive errors
- Regression usually occurs in the first year
- May not lead to spectacle independence
- Other options are phakic IOLS
- Clear lens exchange
- Children with neurobehavioral disorders ( visual autism) that preclude spectacle correction improve vision and global functioning

# Contact Lens Correction of Aphakia in Children

- Silicone elastomer (SE) of high oxygen permeability
- RGP (rigid gas permeable)
- SilSoft Super Plus (B&L) high plus powers and wear on extended wear basis remove once every 30 days with +23, +26,, +29 and +32 with BC 75.,7.7,7.9mm
- Lower-power SE (SilSoft Aphakic, B &L) 1 D increments +11.50 to 20.00 D) BC 7.5 to 8.3mm)
- SE lenses with limited astigmatic correction beyond 2 D)
- RGP can be customized for any power, base curve or diameter.
- Can correct up to 6 D astigmatism, more durable and lower cost
- Not optimal for extended wear.
- RGD more difficult to handle and more frequent replacement.
- SE lenses with more microbial keratitis most likely related to extended wear. Microbial keratitis very low (<1%)

# Frequency of Visual Deficits in Children with Developmental Dyslexia

- Developmental dyslexia (DD): specific learning disability of neurobiological origin with a core cognitive deficit that involves language processing
- Functional imaging studies find abnormalities in processing and word recognition
- DD show slow and inaccurate word recognition and spelling are found in an individual with normal intelligence and sensory abilities
- 7% of the population are affected by DD
- Evidence based treatments revolve around reading strategies and instruction in phonics
- Assess the frequency of visual defects (vergence, accommodation, ocular motor tracking) in children with DD compared with a group of typical developing (TD) readers
- One large study showed minor abnormalities in stereo acuity but otherwise normal visual function.
- Others have shown varied results when examining saccades, vergence and accommodation. Some show convergence insufficiency others no deficits.
- Visual deficits were higher in DD group than in TD group
- The association with reading is less certain
- Eye exercises improve vergence accommodation, and tracking but effects on reading metrics need further study.

# Oculoplastics

# Orbital Blowout Fractures

- Blunt orbital trauma results in blowout fracture of orbital floor or medial orbital wall
- Pediatric trapdoor fractures warrant immediate repair to prevent oculo-cardiac reflex and muscle fibrosis
- Twi issues in debate: the indications and timing of repair
- Study: radiologic findings in untreated patients with changes in boney contour, new bone formation and decreased orbital volumes
- Result: large portion of untreated patients showed improvement in radiology findings consistent with spontaneous improvement clinically.
- Size of the unoperated fracture on imaging decreases with time as the edema resorbs and bone remodels
- Patients undergoing repair showed no difference in outcomes if surgery delayed beyond 2 weeks
- Diplopia may resolve spontaneously and without definite muscle entrapment directly then observe. Many will observe spontaneously

# Retinal Imaging

Deep Learning Applications

# Deep Learning (DL) for Detailed Severity Classification AMD

- Two clinical grading systems for AMD from AREDS: 4-step and 9-step
- Predict 5-year risk of progression to advanced stages
- 4-step easier for highly trained fundus photograph graders but less predictive.
- 9-step requires highly trained graders
- DL AMD grading for 4-step classification performance comparable to human
- DL AMD promising results for 9-step classification
- DL has potential to assist physicians for individualizes detailed risk assessment, clinical studies of disease progression, public screening

# Prediction of Cardiovascular risk factors from retinal fundus photographs via Deep Learning

- Google Research
- Medical images have a wide variety of features, patterns colors values and shapes
- DL learning model trained on 284,335 patient fundus photos
- Two independent data sets 12,026 and 999 patients
- Predicted cardiovascular risk factors not previously thought present or quantifiable in retinal images
- Age (within 3.36 years)
- Gender (AUC=0.97)
- Smoking status (AUC=0.71)
- Systolic blood pressure (within 11.23 mmHG)
- Major adverse cardiac events (AUC=0.70)
- DL training model used anatomical features of optic disc or blood vessels to generate prediction
- Deep learning can extract new knowledge from retinal fundus images

# Miscellaneous Topics

# Povidone-Iodine plus Dexamethasone for Adenoviral conjunctivitis

- PVP-I 0.6% and dexamethasone 0.1% topical
- 144 Patients with positive AdenoPlus test 3 groups: PVP-I plus dex, PVP-I alone, vehicle only
- 3,6 and 12 days after treatment examined and viral cell culture assay
- patients with clinical resolution at day 6 was 31.3% in PVP-I dex 10.9% vehicle group and 18% PVP-I group
- Negative cells culture at day 6 79.2% PVP-I plus dex, 56.5 vehicle and 62% PVP-I alone

# Disinfecting and Calibrate Goldman Applanation Tonometer

- 10% bleach for 5 minutes is recommended.
- Bleach eliminated a broad spectrum of microorganisms.
- Bleach is only method than consistently inactivated adenovirus and HSV
- All disinfectants have been identified as causing tonometer prism damage that may result in patient injury
- All prism have an expiration date and should be discarded after that date.
- Disposable single use applanation tips are available (Tonosafe and Tonomate ) cost >$1 per tip.
- Calibration error tested at 1,20 and 60mm HG and need to be within +/- 1 mmHg.
- New tonometers checked twice the first year then monthly after

# Medicare Part B Spending and Anti-VEGF Drugs

- Ranibizumab (Lucentis) and aflibercept (Eylea) account for 12% of Medicare Part B budget
- Switching from Eylea and Lucentis would save $2.87 billion in 2015 alone.
- 2011 annual Medicare Part B spending $1.43 billion for 671,869 injections for ranibizumab
- 2015 $1.15 billion for 573,796 injections ranibizumab
- For aflibercept 2013 $1.08 billion for 513,836 injections
- 2015 $1.81 billion for 866,749 injections
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# Endophthalmitis Following Bilateral Same-Day Anti-VEGF injection

- Examined results of over 100,000 bilateral same-day anti-VEGF injections.
- % year period for 5890 patients for 50,966 patient visits
- Ranibizumab for AMD and Aflibercept for DME
- 28 cases (0.027%) cases of unilateral endophthalmitis and no instances of bilateral endophthalmitis
- No patients experienced more than a single occurrence
- Demonstrating safety of bilateral same-day anti-VEGF injections

# Herpes Zoster Eye Disease Update

- 1.2 million new cases annually in US with increasing incidence over last 40 years. Caused by reactivation of varicella-zoster virus. 10-20% involving forehead.
- Efforts to combat vision loss: vaccination to long-term suppression
- Herpes Zoster (HZ) more frequently seen in younger individuals and 90% immunocompetent
- The increase in incidence occurred before childhood varicella vaccination
- Ocular involvement 65%, 57% with conjunctivitis; keratitis in up to 12%.
- 25% of patients experience chronic or recurrent disease 5 years later
- Zostavax 2006 live attenuated vaccine immunocompromised cannot have the vaccine. Antivirals need to be stopped. May cause reactivation of HZ keratitis. Decreases burden of disease by 61% and post herpetic neuralgia (PHN) by 66%
- Efficacy wanes to 4 % after 8 years

# Herpes Zoster

- Shingrix adjuvanted HZ subunit vaccine recommended for all immunocompetent individuals 50 and older
- Includes those that have had HZ in past
- Not a live virus; requires two separate injections 2-6 months apart
- 97% efficacious and after 4 years 88% effective
- 91% effective against PHN
- Acute therapy high dose antiviral for one week given within 72 hours of rash
- Chronic and recurrent disease management: prolonged antiviral prophylaxis with Valtrex 500 mg daily and acyclovir 400mg twice daily decrease recurrence by 35%

# New App for Plaquenil Dosing

- DoseChecker App available in Apple App store with iOS operating system
- Prescribing physician enters patient weight, and height and the recommended weekly dosing is calculated
- AAO recommends Plaquenil daily dosage less than 5.0mg/kg actual body weight
- Ideal body weight formulas tend to overdose slight individuals especially women
- Real body weight predicts risk more accurately across all body types

# Visual Rehabilitation

- Closed circuit TV and video magnifiers
- Talking devices including watches, scales, timers liquid level indicators
- Smartphone, tablets, computers e-readers with large print sizes and reverse polarity (white text on black background)tablet offer magnification, text to speech, voice recognition (Siri)and photography without requiring precise focusing
- 
- APPS TapTapSeethat identify object aloud
- Seeing AI scans barcodes
- Smart speakers (Alexa, google home, Echo)offer audio access to weather, news music information
- Rode services Uber Go Go Granny, Lyft
- Fully autonomous vehicles?

# Vision Rehabilitation

- Head mounted devices: magnify at various distances offer broad clear view compared with magnifier or telescope
- Examples: IrisVision, Nu Eyes, E-Sight
- OrCam camera mounted to eyeglass frame offers text to speech capability and audio descriptions of objects and people
- AIRA subscription service connects person with vison loss to live agent wearing smart glasses
- Knows location by GPS and can assist with navigation, finding objects and doing tasks
- Patients with significant visual field loss GPS in smartphones (Blindsquare) vibrate (iWatch) assist in way of finding
- High tech white canes using ultrasound
- Script talk audio medication labels
- DAISY (Digital Accessible Information System) 600,000 free/low-cost digital format audiobooks

# Adaptive Optics

- Employed to overcome inherent optical imperfections of the eye
- AO ophthalmoscope use a wavefront sensor to measure ocular aberrations and correct for them
- AOSLO photoreceptor imaging
- AO ophthalmoscopy offers structural detail on ta cellular level
- Photoreceptor metrics employed to date with cone density for a given eccentricity being most widely used usually compared with normative histology or imaging studies such as OCT
- Others: cone spacing, mosaic geometry, reflectivity and preferred orientation of cones
- Uses in Inherited retinal diseases
- Uses for advice on prognosis, management of inherited retinal diseases