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PACIFIC UNIVERSITY COLLEGE OF OPTOMETRY
2016 VICTORIA CONFERENCE
July 21 to 24, 2016
Delta Victoria Ocean Point
Victoria, B.C. CANADA
COPE EVENT #111397

Date	Speaker	*Title*	COPE	Verification
Thursday, July 21, 2016	Kathleen Elliott, OD	*Pediatrics/Geriatrics – Take Your Pick (2 hrs)*	42824 GO	2 hours
	Jeffrey Urness, OD	*Implications of Selected Corneal Conditions on Refractive Surgery (2 hrs)*	49516 AS	2 hours Therapeutic
	Amber Giannoni, OD	*Environment, Diet and Supplements: What Role Do They Play in Dry Eye Disease? (1 hr)*	40852 AS	1 hour Therapeutic
Friday, July 22	Amber Giannoni, OD	*Dry Eye and Systemic Disease (2 hrs)*	40851 SD	2 hours Therapeutic
	Kathleen Elliott, OD	*The ABC's of Pediatric Eye Care (1 hr)*	49515 FV	1 hour
	John McGreal, OD	*New Ideas in Glaucoma Management (2 hrs)*	43612 GL	2 hours Therapeutic
			Total hours offered: 10	Total hours earned:

Name_____ License #_____

Mailing Address_____

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Please retain a copy of this stamped form as verification of hours earned. Please be advised that your individual state board makes the final determination of applicable hours. For more information, contact Pacific University College of Optometry, 2043 College Way . Forest Grove, OR 97116 . 503-352-2202

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Date	Speaker	*Title*	COPE	Verification
Saturday, July23	John McGreal, OD	*The Latest Trends in Contemporary Medicine (2 hrs)*	43497 PH	2 hours Therapeutic
	Kathleen Elliott, OD	*Non-Surgical Radiofrequency Periocular Soft Tissue Rejuvenation (2 hrs)*	46927 AS	2 hours Therapeutic
	John McGreal, OD	*New Tools for the Tool Box (1 hr)*	42998 GO	1 hour
Sunday, July 24	Jeffrey Urness, OD	*Bacterial Corneal Ulcers (1 hr)*	49517 AS	1 hour Therapeutic
	Kathleen Elliott, OD	*Pediatric Case Reports: The Good, Bad and Ugly (1 hr)*	49514 FV	1 hour
	Amber Giannoni, OD	*Setting Up a Dry Eye Practice (1 hr)*	43552 PM	1 hour
	Jeffrey Urness, OD	*Corneal Transplantation Front to Back, Side to Side.*	40409 PO	2 hours Therapeutic
			Total hours offered: 10	Total hours earned:

Name_____License #_____

Mailing Address_____

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2016 Victoria Conference - July 21 to 24				
Wed	Thursday 7/21	Friday 7/22	Saturday 7/23	Sunday 7/24
	COPE ID: 42824-GO Pediatrics/Geriatrics-Take Your Pick Kathleen Elliott 8:00 am to 10:00 am pages 7 - 10	COPE ID: 40851-SD Dry Eye and Systemic Disease Amber Giannoni 8:00 am to 10:00 am pages 39 - 68	COPE ID: 43497-PH The Latest Trends in Contemporary Medicine John McGreal 8:00 am to 10:00 pm Pages 91 - 112	COPE ID: 49517 AS Bacterial Corneal Ulcers Jeffrey Urness 8:00 am to 9:00 am Pages 142 - 153
				COPE ID: 49514 FV Pediatric Case Reports: the Good, Bad, and Ugly Kathleen Elliott 9:00 am to 10:00 am Pages 154 - 156
	COPE ID: 36382-AS Implication of Selected Corneal Conditions on Refractive Surgery Jeffrey Urness 10:00 am to Noon pages 11 - 23	COPE ID 49515 FV The ABCs of Pediatric Eye Care Kathleen Elliott 10:00 am to 11:00 am pages 69 - 73	COPE ID: 46927 AS Non-Surgical Radiofrequency Periocular Soft Tissue Rejuvenation Kathleen Elliott 10:00 am to Noon pages 113 - 125	COPE: 43552 PM Setting Up a Dry Eye Practice Amber Giannoni 10:00 am to 11:00 am Pages 157 - 174
		COPE ID: 43612-GL New Ideas In Glaucoma Management (2) John Mcgreal 11:00 am to 1:00 pm Pages 74 - 90		COPE ID: 40409-PO Corneal Transplantation Front to Back Side to Side Jeffrey Urness 11:00 am to 1:00 pm pages 175 - 190
ARRIVAL RECEPTION Arbutus Foyer 6:00 pm to 7:00 pm	COPE ID: 40852-AS Environment, Diet and Supplement Amber Giannoni Noon to 1:00 pm Pages 24 - 38		COPE ID: 42998-GO New Tools For The Tool Box John McGreal 12:00 to 1:00 Pages 126 - 141	

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A SANOFI COMPANY

Amber Gaume Giannoni, OD, FAAO
Clinical Associate Professor
University of Houston College of Optometry (UHCO)

Dr. Gaume Giannoni earned her optometry degree from UHCO and completed a Post-Doctoral Fellowship in Cornea and Contact Lens Research with the Texas Eye Research and Technology Center the following year. She is a Diplomate of the American Board of Optometry, a Fellow of the American Academy of Optometry and is certified in Texas as an Optometric Glaucoma Specialist. She is on the Editorial Board for *Advanced Ocular Care* and is a journal reviewer for *Optometry* and *Optometry and Vision Science.* Dr. Gaume Giannoni writes a recurrent dry eye column in *Contact Lens Spectrum* and is also a contributing editor for *Ocular Surface News* and is the Founding Director of the Dry Eye Center at the University Eye Institute where she sees specialty dry eye patients.

Kathleen Foster Elliott, OD, Dipl.ABO
Optometric Director
His Vision for Children Clinic
Tulsa, Oklahoma

Dr. Elliott graduated with honors from NSUOCO. She completed a residency in Ocular Disease Management and went on to complete a two year post graduate study program in Pediatrics with pediatric ophthalmology in Tulsa, OK, where she now practices. She was clinical director at a cataract /refractive surgery co-management center from 1994-1998. Dr. Elliott also co-owned and operated a successful private practice and hospital based clinic in rural Oklahoma from 1998-2010. Dr. Elliott was recently appointed by Oklahoma's Governor as the first female doctor to serve on the Board of Examiners in Optometry, where she serves as Secretary-Treasurer. She is the former Co- Chair of the state Legislative Committee and was named the Oklahoma Legislative Physician of the year for 2012, and received the Oklahoma Optometrist of the Year Award for 2014.

John McGreal, OD
Missouri Eye Associates
St. Louis, Missouri

Dr. McGreal is a graduate of Albright College and the Pennsylvania College of Optometry. He has lectured nationally and internationally for over 20 years on topics ranging from clinical care to compliance/coding. He has been honored as 1998 Missouri Optometrist of the Year and 2005 University of Missouri Educator of the Year. He is currently director of the Missouri Eye Associates, a medical-surgical consultation center in St. Louis. Dr. McGreal is adjunct faculty at the University of California, Berkeley School of Optometry, the Pennsylvania College of Optometry and the University of Missouri.

Jeff Urness, OD, FAAO, ABO
Spokane, Washington

Dr. Urness is a graduate of Pacific University College of Optometry. He completed a residency in Hospital Based Optometry at Northeastern State University College of Optometry. Dr. Urness has served as a consulting optometric physician in SE Washington for twenty years. Working in one of the few corneal services in eastern Washington, Dr. Urness has developed an interest in and an affinity for management of patients with corneal disease and corneal transplants. He is also an adjunct clinic professor for Pacific University's College of Optometry providing education to optometry students, residents and practicing optometric physicians. Dr. Urness presently serves on the optometric staff at the Manns -Granstaff VA Medical Center in Spokane Washington.

Elaine Pedersen, B.Comm., CHRP
Optometric Services Inc.

Ms. Pedersen is the National Training Coordinator for Optometric Services Inc., Canada's largest buying and multi-service group for optometrists. An accomplished speaker, Elaine has given over 300 seminars to optometrists, optometric assistants and opticians across Canada. She holds a Masters of Arts in Leadership from Royal Roads University and a Bachelor of Commerce, specializing in marketing from the University of British Columbia. Ms. Pedersen is also a Certified Human Resources Professional and Myers-Briggs certified.

Carole Timpone, OD, FAAO, FNAP
Associate Dean for Clinical Programs
Pacific University College of Optometry

Her areas of interest, research, and expertise include ocular disease, glaucoma and primary care optometry. Dr. Timpone served as the director of the Pacific University Vision Clinic in Portland for more than 15 years. Since 2013 she has served as the Associate Dean of Clinical Programs at Pacific University.

CONFERENCE STAFF

Jeanne Oliver, Director of External Relations
Victoria Conference Director
jeanne@pacificu.edu

Marti Fredericks
Dir. of Externships & Residency Management
frederim@pacificu.edu

Pediatrics/Geriatrics- Take Your Pick!

Kathleen Foster Elliott, OD, Dipl.,ABO;
George Foster, OD, and Les Walls,OD,MD

Geriatrics

- Systemic , Biological, and Physiological Changes with Aging
- Demographics,Over 30 pts,Hospitalizations,Health Care Consumption,

Geriatrics

- Primary aging over 65,Organ system reserve,Homeostatic Reserve
- Secondary aging:Controllable/Reversible,Prevention keys,

Geriatrics

- Role of Health Care Providers,Basic Physiology aging changes
- Gaining a Background in Medical Aspects of Geriatrics in regards to Systemic Disease

Geriatrics

- Theories on Etiology of aging,free radical, Apoptosis,Genetic,Polygenic,Life Expectancy,

Case reports

- Skin,Orthopedic,Neurologic,Cardiovascular,Auditory,Hypertension,Diabetes,Thyroid DZ,Immune System,Autoimmune,Cancer,

Aging and the Eye

- Medication Problems
- AMD

Pediatrics

- Pediatric population and Optometric practices

Case Reports

- Eyelid Disorders,Diabetes,
- Retinoblastoma,Retinal Hemorrhages , Ocular Trauma

Pediatrics

- The Impact of Geriatrics and Pediatrics on the practice of Optometry

ACA , Medicaid and Medicare Implications

- Video ACA

Patient Needs

- Vision Therapy/Low Vision Clinical Needs
- incorporating into practice

Conclusion

- Gaining Insights for Improving Eye Care to Geriatric and Pediatric Patients
- Video on Exam Techniques

Conclusion

- Questions?
- Thank You

I will praise thee; for I am fearfully and wonderfully made!
Psalm 139: 14

Implication of Selected Corneal Conditions on Refractive Surgery

Objectives

- Review pertinent anatomy
- Review diagnostic characteristics that impact surgical decisions
- Discuss preoperative management
- Demonstrate surgical management
- Present postoperative management

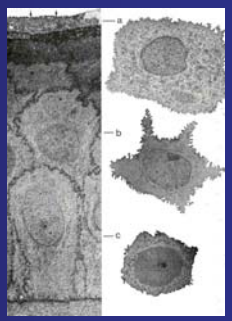
Corneal Anatomy

- Tear Film (7-10 um)
  - Lipid (0.1 um)
  - Aqueous (7-10 um)
  - Mucin (0.02-0.05 um)

- Tear Film Dynamics
  - TBUT (>15s)
  - Schirmer/Phenol Thread (>10mm)

Corneal Anatomy

- Epithelium (50um, 8%)
  - Histology/Morphology
  - Function
  - Reproduction
  - Migration
  - Remodeling



Corneal Anatomy

- Epithelium (50um, 8%)
  - Histology/Morphology
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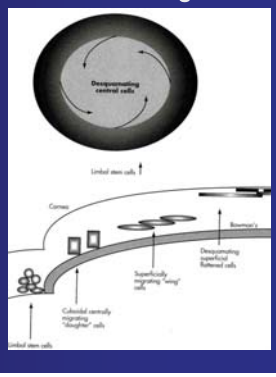
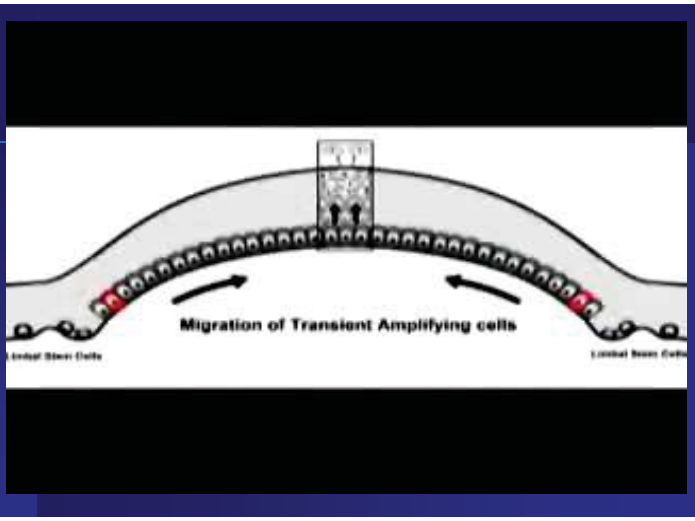
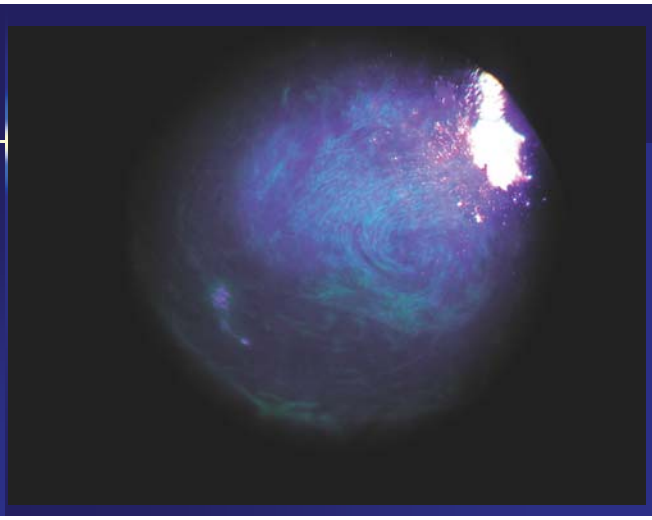
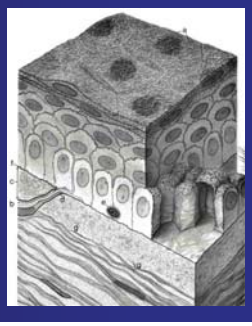






Corneal Anatomy

- **Bowman's Layer** (12um, 2%)
  - Histology/Morphology
  - Repair/Remodeling
  - Function

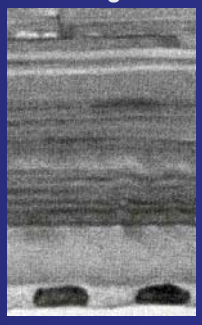


Corneal Anatomy

- **Stroma** (500um, 90%)
  - Histology/Morphology
  - Repair/Remodeling
  - Function

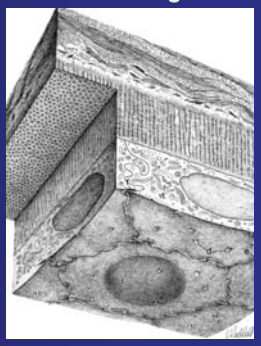
Corneal Anatomy

- **Descemet's Layer** (7um, 1%)
  - Histology/Morphology
  - Remodeling/Repair
  - Function



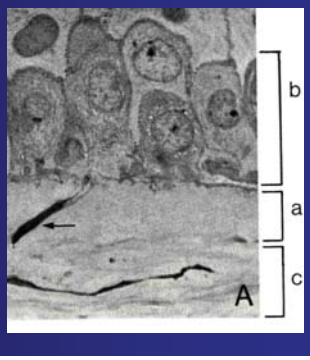
Corneal Anatomy

- **Endothelium** (5um, 1%)
  - Histology/Morphology
  - Reproduction
  - Repair
  - Function



Corneal Anatomy

- Neurons
  - Histology
  - Reproduction
  - Function

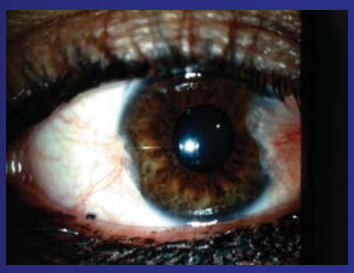


Corneal Anatomy & Physiology

- Tear Film (7-10um)
- Epithelium (50um, 8%)
- Boman's Layer (12um, 2%)
- Stroma (500um, 90%)
- Descemet's Membrane (7um, 1%)
- Endothelium (5um, 1%)
- Neurons (500 trunks)

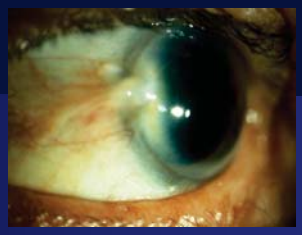
Pterygium

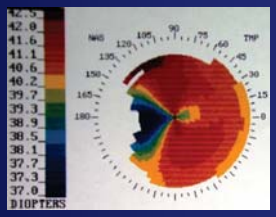
- Stable or active
- Optical impact
- Is there concurrent disease?
  - Lid
  - Lacrimal



Pterygium

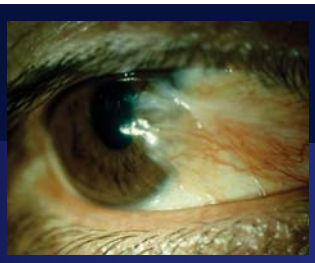
- Stable or active
- Optical impact
- Is there concurrent disease?
  - Lid
  - Lacrimal

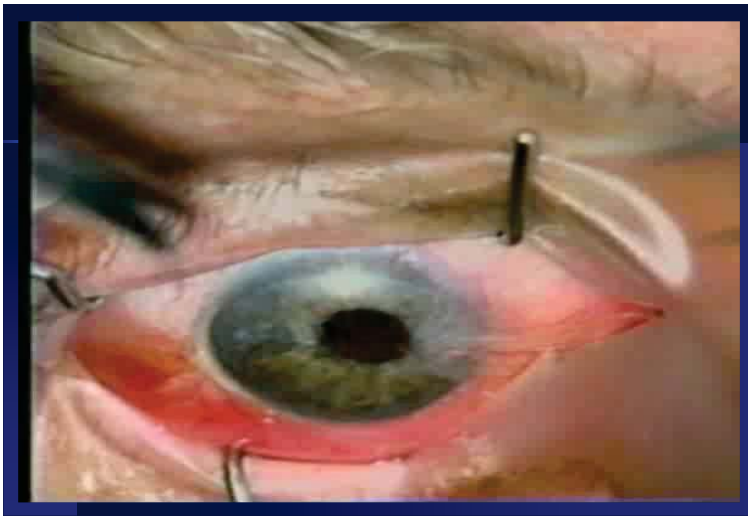




Pterygium

- Surgical management
  - Reduce and stabilize corneal astigmatism
  - Excision with or without graft
  - Excision without or with Mitomycin
  - Expected post op course
    - 1day
    - 1week
    - 1month



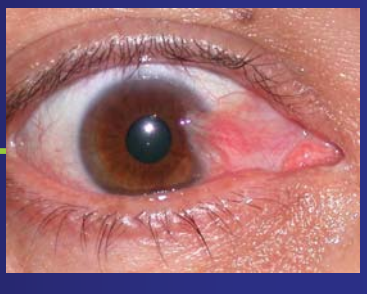


Pterygium

- Surgical management
  - Post op comanagement
    - Medications
      - Pain
      - Antibiotic
      - Anti-inflammatory
      - Lubrication & protection

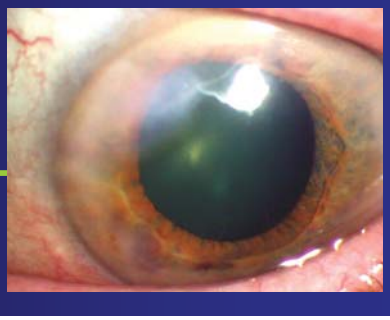
Pterygium

- Impact on cataract & lensectomy
- Impact on LASIK & PRK
- ? need for PTK



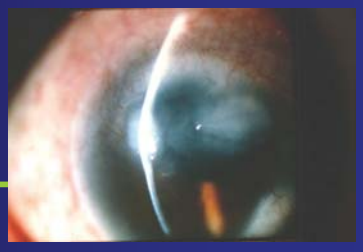
Salzmann's degeneration

- Etiology / Histo-pathology
- Stable or active
- Optical impact
- Is there concurrent disease



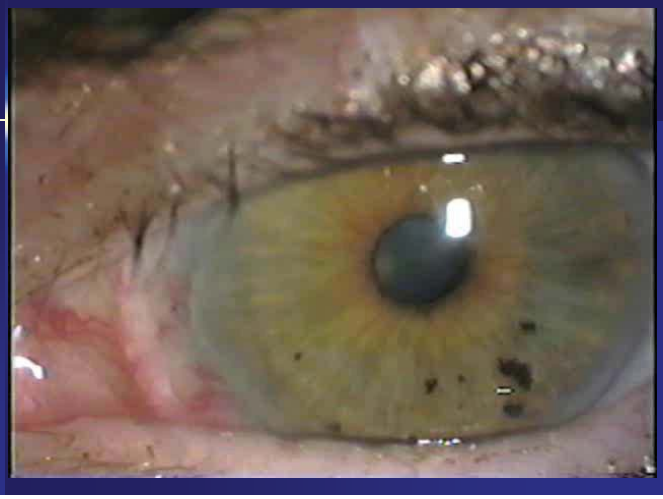
Salzmann's degeneration

- Surgical management
  - Excision
  - Polishing
  - ? Mitomycin
  - Bandage contact lens (BCL)



Salzmann's degeneration

- Expected post op course
  - 1 day
  - 3 day
  - 1 week
  - 1 month
- Post op comanagement
  - Medication
  - Impact of BCL

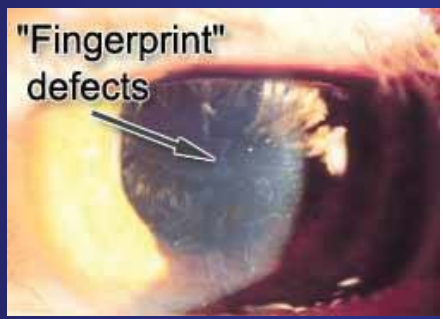


Salzmann's degeneration

- Impact on cataract & Lensectomy
- Impact on LASIK & PRK
- Indications for PTK

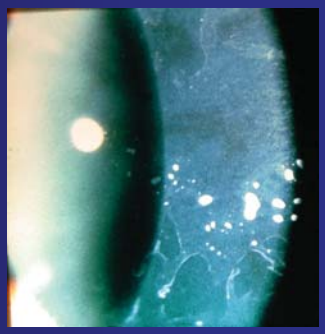
Epithelial Basement Membrane Dystrophy

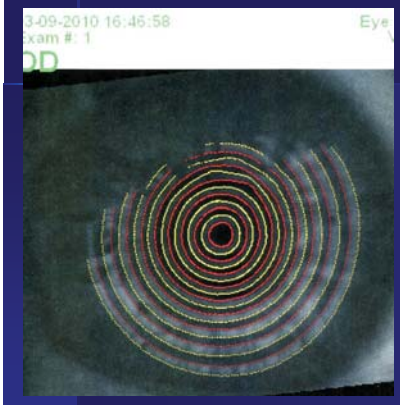
- Etiology / Histo-pathology
- Severity
- Optical impact

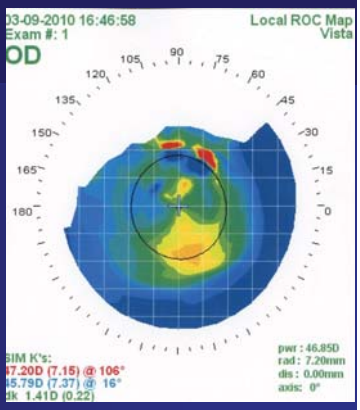


Epithelial Basement Membrane Dystrophy

- Surgical management
  - Debridement
  - Polishing
  - PTK
  - Bandage contact lens
  - (BCL)

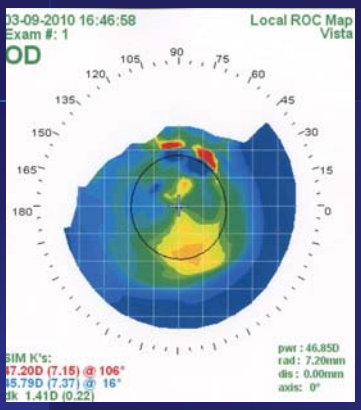


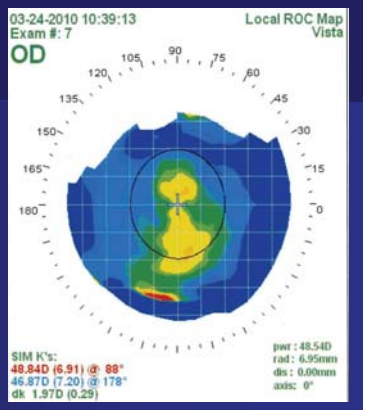


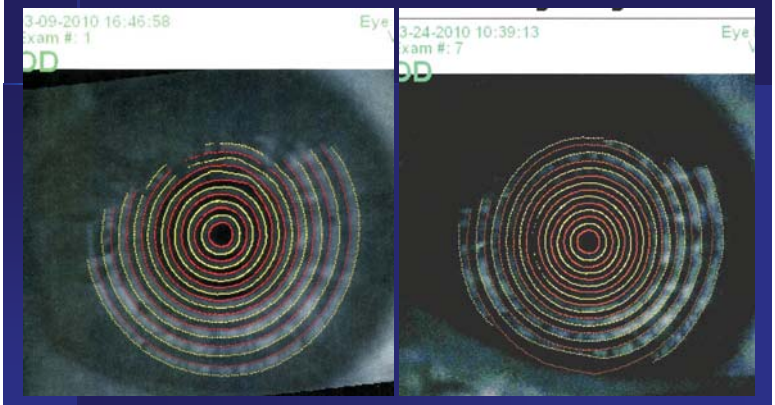


Epithelial Basement Membrane Dystrophy

- Expected post op course
  - 1 day
  - 3 day
  - 1 week
  - 1 month
  - 1 year
- Post op comanagement
  - Medication
  - Impact of BCL





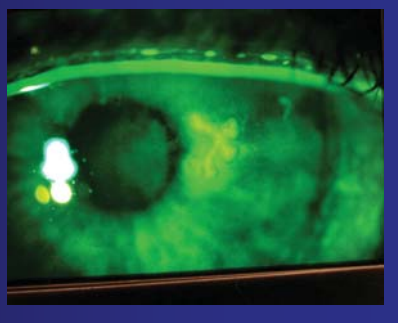


Epithelial Basement Membrane Dystrophy

- Impact on cataract & Lensectomy
- Impact on LASIK & PRK

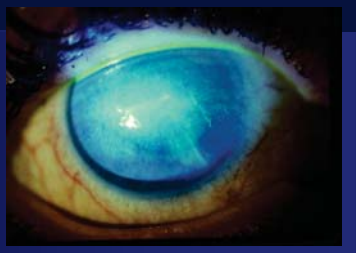
Other Anterior Corneal Conditions

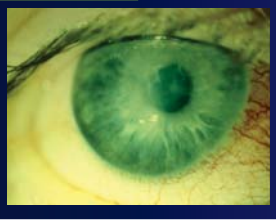
- Epithelial Herpes Simplex
  - Nature, Location & Extent of any scarring
  - Degree of neurotrophy
  - Duration of inactivity
  - Prophylaxis with surgery



Other Anterior Corneal Conditions

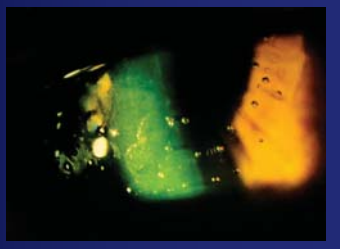
- Neurotrophy
  - Diabetic
  - Herpetic
  - Traumatic
  - Other





Other Anterior Corneal Conditions

- Recurrent Corneal Erosion
  - PRK / PTK (Surface laser Tx)
  - RLE (Refractive lensectomy)
  - ICL (Intraocular contact lens)
  - Leary of LASIK

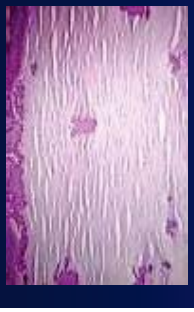


Other Anterior Corneal Conditions

- Other anterior dystrophies
  - Reis-Buckler

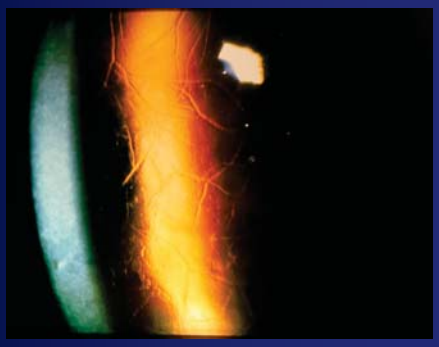
Stromal Dystrophies

- Granular



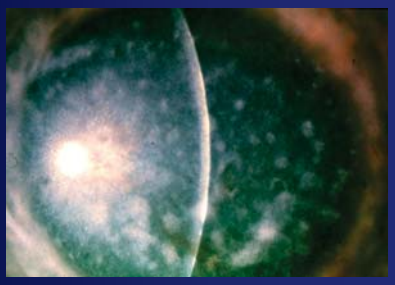
Stromal Dystrophies

Lattice



Stromal Dystrophies

- Macular



Stromal Dystrophies

- Surgical management
  - PTK (maximum treatment depth)
  - ? Mitomycin
  - PKP

Post Penetrating Keratoplasty LASIK/PRK

- Surgical management
  - LASIK & relaxing incision following PKP
    - 15 to 18 months post PKP
    - Suture(s) out
    - Refraction stable
  - Staged surgery
    - Flap and relaxing incision
    - Laser keratectomy

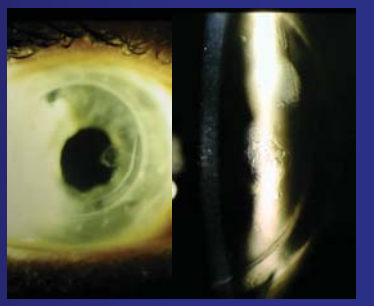
PKP: Staged LASIK Relaxing Incision

Post Penetrating Keratoplasty LASIK/PRK

- Expected post op course
  - 1 day
  - 3 to 5 day (PRK)
  - 1 week
  - 1 month (anticipate enhancements)
  - 3 month

Post Penetrating Keratoplasty LASIK/PRK

- Post op comanagement
  - Medication
  - Epithelial ingrowth
  - DLK
  - Vigilance for rejection
  - Vigilance for reactivation of Herpetic disease
  - Patient expectation



Post Penetrating Keratoplasty Cataract

- Impact on cataract/RLE surgery
  - Timing for surgery
  - IOL selection
  - Target refraction
  - Surgical approach
  - Patient expectation

Post LASIK/PRK Cataract

- Impact on cataract surgery
  - Timing for surgery
  - IOL selection
  - Target refraction
  - Patient expectation

THANKS FOR COMING

ENVIRONMENT, DIET AND SUPPLEMENTS

Victoria, 2016

Amber Gaume Giannoni, OD, FAAO, Diplomate (ABO)
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DISCLOSURES

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  - Vistakon
  - Allergan
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I have no financial or proprietary interests relative to this presentation

Environment, Diet and Supplements

LECTURE OBJECTIVES:

- Educate and remind the practitioner about environmental and dietary factors that can substantially influence the dry eye patient
- Discuss how to educate patients on home/environment modification

OVERVIEW:

I. **Dry Eye Disease (DED)**
II. **Environment and DED:**
  - Climate
    - Humidity, wind, temperature, forced air
    - Intervention strategies
  - Allergens, Air Pollution
    - Elimination, hygiene

III. **Intake and DED:**
  - Water, caffeine, alcohol
  - Oral medications
  - Smoking
  - Diet: pro-inflammatory/anti-inflammatory omegas
    - Supplements

LECTURE OVERVIEW:

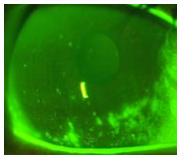
III. Other Factors Associated With DED

- Computer use
  - Ergonomic solutions
  - Blink rate
- Ocular surgery
  - Proactive therapy
  - Post-operative care
- Contact lens wear and care
  - Materials, wear schedule and care
- Ophthalmic medications and artificial tears
  - Toxicity
  - Dosing
  - Supplements

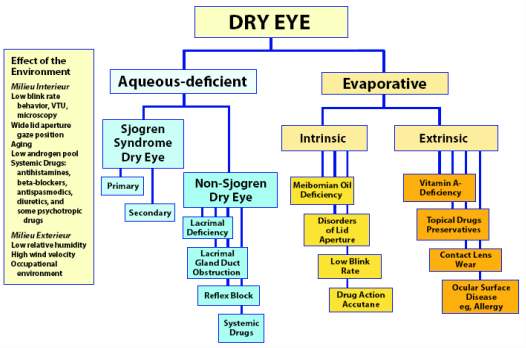
What is "Dry Eye Disease"?

"…multi-factorial disease…symptoms …visual disturbance...potential damage to the ocular surface… increased osmolarity…inflammation of the ocular surface."

(DEWS) 2007



It is a *progressive disease* and the severity of patient symptoms rarely correlate with observed clinical signs.



The Definition and Classification of Dry Eye Disease: Report of the Definition and Classification Subcommittee of the International Dry Eye Work Shop (2007). *The Ocular Surface* 2007;5(2):75-92.

ENVIRONMENT AND DRY EYE Signs and Symptoms:

- Burning, stinging, dry or 'sticky lid' sensation
- Grittiness or foreign body sensation
- Fatigue/discomfort
- Photophobia
- Contact lens intolerance
- Injection/chronic redness
- Increased blink rate
- Epiphora
- Transient blur*

ENVIRONMENT AND DRY EYE: Climate

Humidity

- Depends on temp, water vapor concentration & altitude
- Less at high elevations (i.e. reduced air pressure)
- Less in cold air (i.e. cold air holds less water)
  - Saturated air at 80˚F holds 22x more water than 0°F
  - Colder air increases evaporation pressure

ENVIRONMENT AND DRY EYE: Climate

Humidity

- Wind ↑ evaporation (especially cold wind)
- Re-circulated air ↓ humidity and ↑ airborne bacteria

= **Dehydration**

ENVIRONMENT AND DRY EYE: Climate

Humidity

- Relative humidity < 30% = dry eyes and skin
- Relative humidity < 10% = dry mucosa
- Airplane cabins = ~ 2-15% (drier than Sahara desert)

(Sunwoo et. al, 2006)

ENVIRONMENT AND DRY EYE: Climate

Intervention Strategies:

- Re-direct air vents; stop ceiling fans (night)
- Humidifiers
- Wrap around sunglasses
- Copious oil-based lubricants (day); gel (night)
- Improve MGD

ENVIRONMENT AND DRY EYE: Allergens and Pollution

- 50 million allergy sufferers in the U.S. & Canada
  - 70-80% have ocular allergy symptoms
- Dry eye patients are more at risk – decreased ability to dilute and clear allergens
- Untreated allergy increases inflammation and exacerbates dry eye symptoms

American Academy of Allergy, Asthma and Immunology, 2012; Sign K et. al. 2010

ENVIRONMENT AND DRY EYE: Allergens and Pollution

What you can do……

- Diagnose and treat the allergy!
  - Prescribe a mast-cell stabilizer
  - Consider anti-inflammatory drops
  - Copious artificial tears - refrigeration helps
  - Cold compresses
- Daily disposable contact lenses

ENVIRONMENT AND DRY EYE: Allergens and Pollution

What your patient can do…..

- Wash face/lids/lashes/hair/pillowcases nightly
- Avoid fervent lid scrubs during acute flares – releases more histamine
- Begin mast cell stabilizer several weeks before seasonal allergy symptoms typically begin
- Avoid oral antihistamines, if possible
- See allergist for more targeted control

INTAKE AND DRY EYE: Water

- Chronic dehydration = dry eye (and skin, hair…..)
  - ½ body weight in oz daily + 1 oz/ oz coffee/alcohol/soda

INTAKE AND DRY EYE: Caffeine

- Excess caffeine = diuretic effect
- Was proven to increase tear secretion, but:
  - Study was on normal patients (excluded if they had any disease that affected tear production)
  - Tear production was increased most in subjects with 2 specific genetic variations: (ADORA2A and CYP1A2)

Arita R et. al 2012

INTAKE AND DRY EYE: Alcohol

- Small study (n=20): 2 beers/2 hours in normal subjects:
  - Ethanol in tears 4 hrs after last drink
  - Increased osmolarity @ 4 hrs
  - Decreased tear stability @ 12 hrs
  - Increased corneal staining @ 12 hrs
- Even small amounts of alcohol can have a dramatic effect on the ocular surface of normal patients.

Kim JH et. al. 2012

INTAKE AND DRY EYE: Medications

Antidepressants
Antipsychotics
Anxiolytics
Antihypertensives
Antispasmotics
Antihistamines
Decongestants
Diuretics
Incontinence meds
Retinoids
Opioids
Botox

Educate patients not to stop medically-necessary meds without PCP supervision!

INTAKE AND DRY EYE: Smoking

- 2x greater dry eye complaints in smokers
- Decreased tear stability:
  - Decreased lipid layer (interferometry)
  - Decreased TBUT
- Decreased cornea and conjunctival sensitivity
- Change in tear protein composition

Thomas J et. al 2012; Grus FH et. al 2002

INTAKE AND DRY EYE: Diet/Omegas

Omega 6

- Mostly "Pro-inflammatory"
- Dairy, eggs
- Vegetable oils
- Processed foods
- Meat

Omega 3

- "Anti-inflammatory"
- Cod liver oil
- Cold water/wild fish
- Walnuts
- Flaxseed, chia seed

INTAKE AND DRY EYE: Diet/Omegas

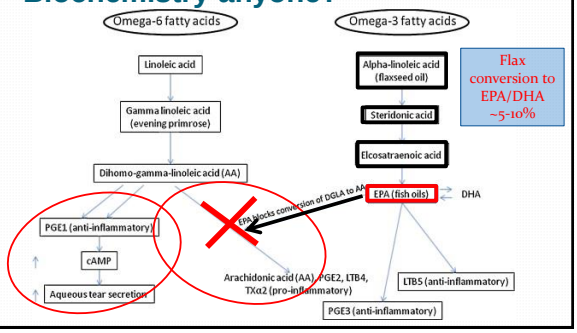
- Want a low Omega 6: Omega 3 ratio
- 1:1 or 2:1 ratio is ideal
- Typical diet is 25:1…….50:1!

INTAKE AND DRY EYE: Diet/Omegas

- Essential fatty acid (EFA) not produced by the body:
  - ALA (Alpha-linolenic): Primarily from flax seed
  - EPA (Eicosapentaenoic Acid): Primarily from fish
  - DHA (Docosahexaenoic Acid): Primarily from fish

- Reduces ocular surface inflammation
- May aid in production of good quality meibum
- Good for skin, hair, nails and GI

INTAKE AND DRY EYE: Biochemistry anyone?



How Much?

INTAKE AND DRY EYE: Diet/Omega 3

Study: Dry Eye Clinical Study Group (DECSG):

- 61 patients using artificial tears for DE symptoms
- Randomized, double-masked trial
  - All subjects: lid hygiene and artificial tears
  - Test subjects: TID dosing of proprietary omega-3 and multivitamin blend (control group: placebo (sunflower oil)
- 12 weeks duration
- D/C all supplements, drops and meds 15 days prior

Olenik A et. al. Clin Ophthalmol Jan 2014

Table 1 Composition of Brudysec® 1.5 g

Composition	Per capsule	% recommended daily amount	Per three capsules	% recommended daily amount
Concentrated oil in ω-3 fatty a			1500 mg	
TG-DHA 70%			1050 mg	–
EPA 8.5%			127.5 mg	–
DPA 6%			90 mg	–
Vitamins				
Vitamin A (retinol)			400 µg RE	50
Vitamin C (ascorbic acid)			80 mg	100
Vitamin E (d-α-tocopherol)			12 mg α–TE	100
Essential trace elements				
Zinc			5 mg	50
Copper			0.5 mg	50
Magnesium			1 mg	50
Selenium			27.5 µg	50
Other components				
Tyrosine	10.8 mg	–	32.5 mg	
Cysteine	5.83 mg	–	17.5 mg	
Glutathione	2 mg	–	6 mg	

Per three capsules

1500 mg Total/day
1050 mg (TG-DHA)
127.5 mg (EPA)
90 mg (DPA)

Note: The percentage recommended daily amount of all nutrients is 250 mg of DHA (Regulation [EU] No. 432/2012 of the European Parliament and of the Council, of 16 May 2012).[9] Brudysec®, Brudy Laboratories, Barcelona, Spain.
Abbreviations: TG-DHA, triglyceride bound docosahexaenoic acid; EPA, eicosapentaenoic acid; DPA, docosapentaenoic acid; RE, retinol equivalents; TE, tocopherol equivalents.

INTAKE AND DRY EYE: Diet/Omega 3

Results:

Both groups showed improvement from baseline in:

- OSDI
- Corneal staining
- Lid margin inflammation*
- TBUT (control 6.94-> 8.05 treatment: 6.45->12.63)*

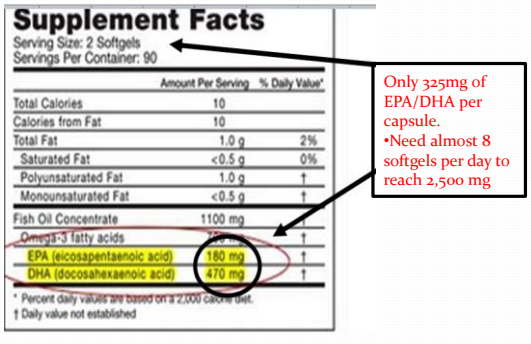
***Statistically significant compared to control group**

INTAKE AND DRY EYE: Diet/Omega 3

Quality and Quantity Matter:

How much should you recommend?

- Recommended: 4000mg per day of EPA+DHA
- Supplement: 1000-3000 mg per day depending on pt
  - "High potency" is usually the most economical
  - Look for at least 700 mg in 1000 mg capsule
- Need to teach patients how to read the labels!



INTAKE AND DRY EYE: Diet/Omega 3

Quality Matters:

- Higher grade formulations:
  - Usually less "fish burps" but higher in cost
  - Almost never available in common retail outlets
    - Nordic Naturals
    - Doctor's Advantage
    - Physicians Recommended Neutraceuticals (PRN)

INTAKE AND DRY EYE: Diet/Omega 3

What about the risk of prostate cancer?

The Selenium and Vitamin E Cancer Prevention Trial (SELECT):
- Evaluated protective effects of Selenium and Vitamin E

Results:
- Those with higher blood levels of long-chain Omega 3s were more likely to have prostate cancer.

EA Klein, et al. JAMA 2011; 306(14) 1549-1556.

INTAKE AND DRY EYE: Diet/Omega 3

Potential problem?

- Conclusions were based on a single blood test:
  - Cancer due to intake factors takes time to develop – simply don't know if there is a direct link
- Most well-designed studies show a reduction in prostate-cancer risk with omega 3 intake

http://www.clspectrum.com/articleviewer.aspx?articleID=108951

INTAKE AND DRY EYE: Diet/Omegas

Patient Education:

- 4-8 wks for symptomatic relief
- Potential for stomach upset
  - Divide into 2 or 3 doses/day
  - Take with food (esp. fatty foods)
- Requires long-term use to maintain results
  - Return of symptoms within a few days of stopping

INTAKE AND DRY EYE: Diet/Omegas

Patient Education:

- Risk of increased bleeding/bruising (>3g/day)
  - Consult with PCP if on blood thinner
  - Educate patient on informing all doctors
    - Upcoming surgery
- Caution in liver disease, diabetics, low b.p.
- What about mercury levels and pregnancy?
  - Several brands tested in a variety of studies – all had negligible levels

INTAKE AND DRY EYE: Diet/Omegas

Other Considerations:

- How much is already in their diet?
- Capsule vs. liquid (difficulty swallowing pills?)
- Added herbal supplements can have unwanted side effects – know what you're prescribing

INTAKE AND DRY EYE: Computer Use

- Blink rate on a computer is reduced approx 60%
  - ~4.5 blinks per minute
- Number of partial blinks increases, which:
  - Decreases tear spreading
  - Decreases allergen elimination
  - Decreases meibomian gland secretion

INTAKE AND DRY EYE: Computer Use

What your patient can do…..

- Lower computer height to narrow fissure width
- Re-direct air vents
- Stay hydrated
- Full blinks
- Visual breaks every 20-30 minutes
- Non-preserved tears every hr
- Reduce glare
  - Windows, lights, AR coating
- Proper Rx

OTHER INDUCED FACTORS Refractive Surgery

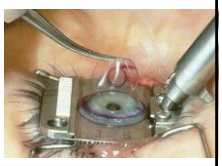
3-6 months post-procedure:

- Neurotrophic cornea
  - Severed feedback loop
  - Results in altered tear flow
- Decreased goblet cell density
  - Loss due to suction ring
  - Often takes 6 weeks to regenerate
  - Some studies show 40-50% loss at 12 mo

OTHER INDUCED FACTORS
Refractive Surgery

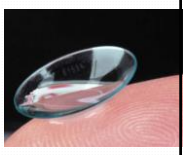
Pre/post-treatment considerations:

- Provocative pre-op SCL 'stress' test
- Omega 3 supplements
- Artificial tears
- Punctal occlusion
- Topical cyclosporin (pre/post)



Surgical outcome is only as good as the cornea/tear film*

OTHER INDUCED FACTORS
Contact Lenses



CL-related dry eye:

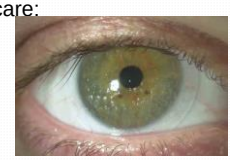
- Increased risk with age/female
- Reported in 65% of SCL wearers
- Largest reason for drop-out
  - No change in drop out rate in 30 years!
  - Single patient dropping out of lenses is estimated to reduce practice lifetime income by $24,000

(Rumpakis, 2010)

OTHER INDUCED FACTORS
Contact Lenses

- Review wear schedule:
  - Compliant? **Rub step?**
  - EW?
  - Discard schedule?

- Review solutions and care:
  - Compliant?
  - Sensitivities?
- CL fit and condition
  - Tight fit?
  - Protein deposits?



OTHER INDUCED FACTORS
Contact Lenses

GENERALLY speaking……

- **Disposable** vs conventional
- **DW** vs EW
- **High Dk** vs low Dk
- **Daily** vs 2 week vs monthly disposal
- **Low water** vs high water
- FDA Group?
  - Group II and IV wearers were 2-3x more likely to report dry eye than **Group 1** wearers.

(Efron and Brennan (1998))

OTHER INDUCED FACTORS
Topical Medications

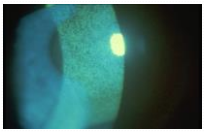
Topical Ophthalmics Often Associated with Dry Eye:

- Glaucoma
- Decongestants
- Antihistamines
- Vasoconstrictors
- Artificial Tears

OTHER INDUCED FACTORS
Topical Medications

BAK effects on the ocular surface:

- ▶Decreases epithelial cell integrity
- ▶ Compromises epithelial barrier
- ▶ Impairs corneal healing
- ▶ Increases inflammation
- ▶ Decreases goblet cells
- ▶ Reduces tear function
- ▶ Decreases tear stability



Main preservative used in most glaucoma meds

OTHER INDUCED FACTORS
Topical Medications

TBUT (Seconds)	Carteolol Without BAK	Carteolol With BAK
Baseline	9.0	10.4
30 minutes later	8.1	7.9
1 hour later	7.3	7.4
3 hours later	7.9	6.1†

Decreased TBUT 3 hours after a SINGLE drop: -1.1 -4.3

Baudouin C et al. *Br J Ophthalmol*. 1998;82(1):39-42.

OTHER INDUCED FACTORS
Topical Medications

BAK Preserved OTC Products

*Trademarks are the property of their respective owners

OTHER INDUCED FACTORS
Topical Medications

Recommend preservative-free AT if:

- Already on several topical drops (i.e. glaucoma)
- Plan on using >qid
- Plan on using long-term
- History of ocular allergy

Switch to BAK-free glaucoma formulations:

- BAK-free travaprost (sofZia)
- Alphagan P (purite)
- Timoptic XE (benzododecinium bromide)
- Preservative free Cosopt (Canda only)

ENVIRONMENT, SUPPLEMENTS and DIET
Actual Case Example:

55 year old; female attorney

- Eyes are dry and chronically red (more so at work)
- Vision is blurry (especially toward the end of the day)
- Has seen 2 other doctors. Both recommended she buy OTC drops that only help for 15 minutes.

ENVIRONMENT, SUPPLEMENTS and DIET
Case Example:

POH: Dryness started a few years ago; progressive
PMH: Menopausal – no current treatment
SH: Smoker x 15 years (1 pk/day)
Meds:

- OTC Clear Eyes several times/day
- OTC Tylenol PM (during the week)

ENVIRONMENT, SUPPLEMENTS and DIET
Case Example:

Environmental/dietary history:

- Drinks coffee all day while at work
- 2-3 glasses H20 daily
- On computer from 8am-6pm
  - One 60 minute lunch break
  - Two 15 minute cigarette breaks.
  - Computer sits slightly above eye level at about 55cm.
- Faces air vent at work; sleeps with ceiling fan and A/C.
- Abundant airline travel
- Reports below average diet (fish once every 2-3 months; eats take-out frequently at desk)

ENVIRONMENT, SUPPLEMENTS and DIET Case Example:

Pertinent exam results:

- Low hyperope with low cyl and presbyopia
  OD: +0.50-0.75x050
  OS: -0.25-0.25x172
  add: +2.50
- Wears +2.50 OTC at the computer - not working well
- No BV issues

ENVIRONMENT, SUPPLEMENTS and DIET Case Example:

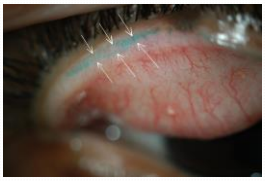
Pertinent slit lamp findings:

- (+) Lid Wiper Epitheliopathy
- (+) Incomplete blink
- Turbid meibum
- Grade 1 inferior corneal SPS (NaFl) OU
- N&T Grade 2 conj. lissamine green staining OU
- Moderate tear prism; low-normal Schirmer's score
- TBUT: 5 sec

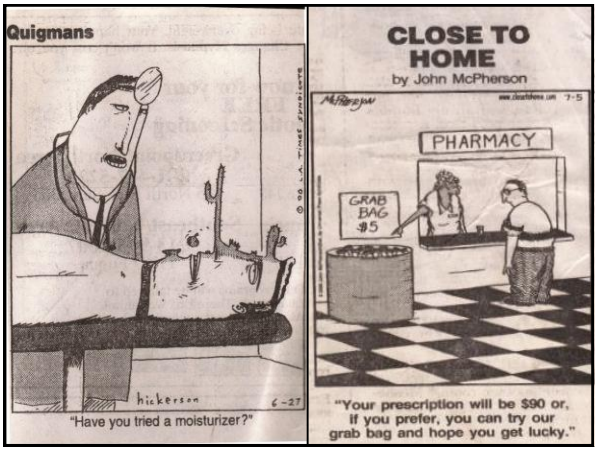
ENVIRONMENT, SUPPLEMENTS and DIET Case Example:

https://www.mivision.com.au/dry-eye-complaints-lid-wiper-epitheliopathy/

Normal staining of subcutaneous junction



Wide, feathery staining in lid wiper epitheliopathy



ENVIRONMENT, SUPPLEMENTS and DIET Case Example: Treatment

Environmental/Dietary Changes:

- STOP SMOKING!
- Lower computer height
- Re-direct air vents
- Frequent visual breaks; complete blinks
- D/C ceiling fan at night and/or try sleep mask or gel
- Increase H_20; decrease caffeine
- D/C OTC "sleep" meds
- Omega 3 supplement (2000mg/day divided dose)

ENVIRONMENT, SUPPLEMENTS and DIET Case Example: Treatment

Other Changes:

- Proper computer specs with correct balance and oblique axis cyl correction:
  - Computer Rx: +1.75-0.75X050 OS +1.00-0.25x172 * ARC
- Non-preserved oil-based tear q 1-2 hr while at terminal
  - Explain WHY this drop will work better than others tried
- Address MGD: Warm compress therapy, Lipiflow
- Add short-term corticosteroid – monitor IOP
- Add Restasis and/or topical testosterone

SCHEDULE a F/U Visit (4-8 weeks)

ENVIRONMENT, SUPPLEMENTS and DIET Case Example: Patient Education

- **Educate**: Ocular effects of smoking
- **Educate**: Menopause and hormone changes
- **Educate**: Airline travel and low humidity environment
- **Educate**: Chronic dehydration
- **Educate**: Decreased blink rate on computer
- **Educate**: Side effects of OTC sleep aids and chronic use of preservatives/vasoconstrictors
- **Educate**: Chronic nature of DES and therapy takes time

ENVIRONMENT, SUPPLEMENTS and DIET

SUMMARY

- Environmental and dietary modifications are often overlooked or ignored in the exam room.
  - "Time consuming/busy practice" – use staff/handouts!
  - "Doesn't make much difference" – false!
  - "It's common sense!" – not true!
- Small changes can be quick, easy and make a huge difference!

DRY EYE AND SYSTEMIC DISEASE

VICTORIA, BC

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I have no financial or proprietary interests relative to this presentation

Objectives

Goals of this lecture:

I. Expand the attendee's knowledge of DED risk factors based on medical and pharmaceutical history
II. Emphasize the importance of early DED intervention in specific populations
III. Improve the attendee's understanding of the sub-types of dry eye most commonly exhibited in certain conditions
IV. Provide insight as to the most effective therapies for specific types of dry eye

Overview:

I. **Overview of Dry Eye Disease (DED)**
   I. Definitions/subtypes
   II. Epidemiology
   III. Quality of life
   IV. Contributing factors
II. **Review of 15 conditions related to DED**
   I. Epidemiology
   II. Dry eye considerations
   III. Ophthalmic management

Overview:

III. **Drugs with known/suspected DED side-effects**
   I. Prescription medications
   II. Over-the-counter medications

IV. **Systemic disease and dry eye in pediatrics**
   I. Juvenile Diabetes
   II. Juvenile Arthritis

PART I: REVIEW

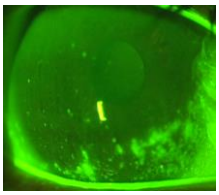
I. **Classification**
II. **Epidemiology**
III. **Quality of life**
IV. **Contributing factors**

What is "Dry Eye Disease"?

"…a multi-factorial ***disease*** **…potential** damage **to the ocular surface…. *increased osmolarity* of the tear film and *inflammation* of the ocular surface."**

-2007 Report of the International Dry Eye Workshop (DEWS)

- **Signs and symptoms rarely correlate**
- **Chronic and progressive**



The Definition and Classification of Dry Eye Disease: Report of the Definition and Classification Subcommittee of the International Dry Eye Work Shop (2007). *The Ocular Surface* 2007;5(2):75-92.

Why I lecture on dry eye….

The average dry eye patient has:

- Waited more than **6** years before seeking care
- Purchased more than **6** types of artificial tears over the past year.
- Visited eye doctor an avg of **6** times since onset
- **92%** are treated with only topical drops or ointments

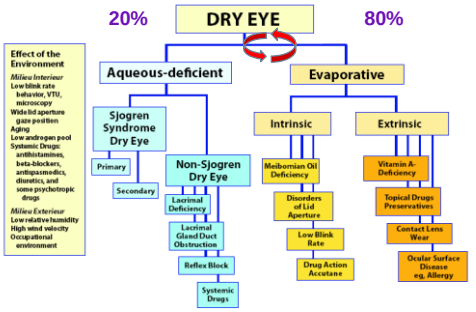
*Gallup Study of Dry Eye Sufferers (2009)

If we aren't asking the right questions and actively looking for DED, we are missing an opportunity to intervene early and change the course of a chronic, progressive disease

Primary Forms:

- **Aqueous Deficient Dry Eye:** Production of aqueous from the lacrimal gland is insufficient to keep the eyes moist
- **Evaporative Dry Eye:** Lipid deficiency caused by meibomian gland dysfunction causes tears to evaporate at a faster rate than normal

DEWS Classification



The Definition and Classification of Dry Eye Disease: Report of the Definition and Classification Subcommittee of the International Dry Eye Work Shop (2007). *The Ocular Surface* 2007;5(2):75-92.

Prevalence

Approx. 10 % in the U.S. and 25% in Canada

DRY EYE PREVALENCE IN THE U.S.

Dry Eye Category	Severe	Moderate	Episodic	Total
Sjögren's Disease	1,427,847	1,223,869	407,956	3,059,672
Post-menopausal Women	1,933,486	3,093,577	7,733,943	12,761,006
Men Over Age 65	518,751	864,585	1,729,169	3,112,505
LASIK Patients	4,722	9,444	141,667	155,833
Past LASIK Patients	34,027	68,053	340,266	442,346
Other	196,924	393,848	2,888,221	3,478,994
Total U.S.	**4,115,757**	**5,653,377**	**13,241,222**	**23,010,355**

[1] Market Scope. 2010 Comprehensive Report on The Global Dry Eye Products Market.

Quality of Life

- Similar to dialysis, angina or hip fracture
- Increased risk of anxiety and depression
- Decreased worker productivity/economic loss
- Higher risk of co-morbidities:
  - Heart, dyslipidemia, stroke, anemia, asthma
  - MG, Lupus, DM, Hypothyroidism,
  - Peptic ulcers, Hepatitis B, Liver Disease

Schiffman RM et. all. 2003; Wang TJ et. al 2010

- Driving
- Reading
- Computer Work
- Recreation……

http://www.fortifeye.com/

AFFECTS ALL ASPECTS OF LIFE

http://www.dailymail.co.uk/health/article-2487732/

Contributing Factors

- Environment (low humidity, A/C, computer, irritants)
- Contact Lens wear and care
- Diet (low vitamin A, low omega 3, alcoholism)
- Neurotrophic corneas (LASIK, HSK, HZK)

- **Age**
- **Gender**
- **Race**
- **Anterior segment diseases (blepharitis, MGD)**
- **Systemic Disease and other conditions**
- **Medications**

Age

Risk increases with age:

- 20% of those >45 yrs **
- 75% of those >65 yrs**

Why? More medications, comorbidities etc.

(Market Scope., 2011; Pray WS, 2006).

Population is aging

Between 2000-2050:

- 65-84 age group will increase by 100%
- 85+ age group will increase by 333%

http://spidersilk-events.com

Gender

- Higher in women than men in all age groups
- ~3.2 million women >50
  - Visit doctor more?
  - Hormone relationship?

(Schaumberg et. al., 2003)

Race

- Caucasians = African Americans (prevalence/severity)
- Hispanic and Asian women > Caucasian women
  - 80% higher incidence of SEVERE dry eye symptoms

http://districtworld.wordpress.com/

Schein OD et. al, 1997
Schaumeberg et al, 2003

BOTTOM LINE….

- Next to ametropia, dry eye will be the most common condition you will see in your office

PART II.
SYSTEMIC CONDITIONS AND DED:

i. **Sjogren's Syndrome**
ii. **Autoimmune connective tissue diseases**
iii. **Sarcoidosis**
iv. **Thyroid dysfunction**
v. **Diabetes Mellitus and Metabolic Syndrome**
vi. Androgen deficiencies
vii. Rosacea/Dermatology
viii. Bell's palsy
ix. Crohn disease
x. Cancer, radiation and chemotherapy
xi. Alcoholism
xii. Fibromyalgia
xiii. Chronic Fatigue Syndrome,
xiv. Parkinson's Disease

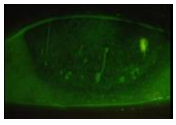
DRY EYE AND SYSTEMIC DISEASE:
Sjogren Syndrome (SS):

Sjogren Syndrome: Definition

Multi-system autoimmune disease characterized by progressive hypofunction of exocrine glands

- ***Primary SS** – occurs alone
- ***Secondary SS** – occurs with autoimmune disease

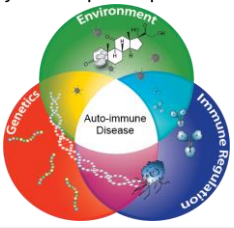
- All tear layers can be affected*

www.Sjogren'ssyndrome.support.org

DRY EYE AND SYSTEMIC DISEASE:
Sjogren Syndrome (SS):

- Combination of genetic, environmental, and hormonal factors
- Viral or bacterial infection is thought to activate the immune system in pre-disposed individuals



Tincani A, et al. 2012 and Ice JA, et al. 2012

DRY EYE AND SYSTEMIC DISEASE:
Sjogren Syndrome (SS):

COMMON PERCEPTIONS:

- SS is an uncommon/rare disease
- Optometrists will rarely see a patient with SS
- SS is so serious that an OD will be unlikely to be the first to diagnose it (i.e. the disease will already be diagnosed by a another health care provider).
- If there isn't significant corneal damage, dry mouth and joint pain, it can't be SS
- If a patient has SS, not much can be done.

DRY EYE AND SYSTEMIC DISEASE: Sjogren Syndrome (SS):

Sjogren Syndrome: Epidemiology:

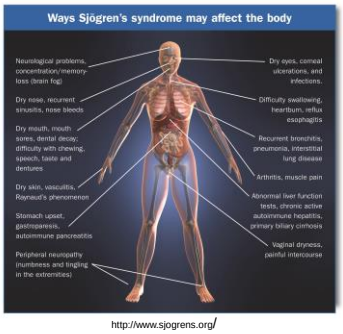
- Occurs in ~1% of the population
- Only 1 in 4 have been diagnosed
- One of the most common autoimmune disease
- 90-95% are females over 40

Venus Williams: diagnosed with SS at age 31

DRY EYE AND SYSTEMIC DISEASE: Sjogren Syndrome (SS):

Average time to reach a diagnosis is **5-7 years**!

DRY EYE AND SYSTEMIC DISEASE: Sjogren Syndrome (SS):



http://www.sjogrens.org/

Systemic effects occur in 30-70% of patients

- Pts don't tell dentist about dry eye….
- Pts don't tell OD about dental decay….
- Pts don't tell GI doctor about memory loss….

(Tincani A, et al. 2012)

DRY EYE AND SYSTEMIC DISEASE: Sjogren Syndrome (SS):

Blood work in patients with Sjogren's Syndrome:

- ANA (+)…….70%
- RF(+)…… 60-70%
- ESR…….. 80% show elevation
- Anti-Ro/SS-A (+)……..60-70%
- Anti-La/SS-B (+)……..40%*

*In SS, the combined sensitivity/specificity of classic blood markers is only 40-60% (Tincani A, et al. 2012)

DRY EYE AND SYSTEMIC DISEASE: Sjogren Syndrome (SS):

Clinical suspicion:

- Symptoms of dry mouth > 3 mo
- Symptoms of dry eye > 3 mo
- Signs of dry eye
  - Low tear prism
  - Significant ocular surface staining
  - Filamentary keratitis
- Autoimmune disease, esp. RA, thyroid dz

* Dry eye and dry mouth can be caused by many factors

DRY EYE AND SYSTEMIC DISEASE: Sjogren Syndrome (SS):

New Diagnostic standards* (eliminated subjective criteria)

- Significant ocular surface staining in 1 eye
- (+) Minor salivary gland biopsy (i.e. lip)
- (+) Blood work, either:
  - (+) Anti-SSA/Ro or (+) Anti-SSB/La antibodies OR
  - (+) Rheumatoid Factor AND (+) ANA titer (>1:320)

➢ **2 of 3 criteria above must be present**

***Sjogren's International Collaborative Clinical Alliance (SICCA)…endorsed by America College of Rheumatology**

DRY EYE AND SYSTEMIC DISEASE: Sjogren Syndrome (SS):

New Blood Markers for Sjogren syndrome?

- Includes traditional biomarkers
- 3 new proprietary markers
- Claim to increase early detection and cumulative specificity to 92.1%

Bausch & Lomb

DRY EYE AND SYSTEMIC DISEASE: Sjogren Syndrome (SS):

MANAGEMENT:

- Copious lubricants (drops, gels, ointments, inserts)
  - Tears with hyaluronic acid may be more effective (Baudouin, 2004)
  - Use non-preserved formulations
- Humidifier; Moisture chamber goggles
- Punctal occlusion (silicone or cautery)
- Topical corticosteroids (pulse therapy)
- Topical ophthalmic cyclosporine

DRY EYE AND SYSTEMIC DISEASE: Sjogren Syndrome (SS):

MANAGEMENT:

- Filament removal/bandage lens/amniotic membrane
- Compounded mucolytics
- Therapeutic lenses (i.e. SCL, scleral lenses)
- Autologous serum
  - Contains EGF, Vitamin A, fibronectin etc
- Topical or systemic androgen
  - May suppress lacrimal gland inflammation and improve MGD

DRY EYE AND SYSTEMIC DISEASE: Sjogren's Syndrome (SS):

SYSTEMIC PRESCRIPTIONS:

Oral cholinergic parasympathomimetic agonists

- Stimulate cholinergic receptors to increase tear and saliva production
- May also act on cardiac muscle and smooth muscle
  - Side effects (non-inclusive):
    - Headache
    - Sweating
    - Nausea, diarrhea,
    - Irregular heart beat

DRY EYE AND SYSTEMIC DISEASE: Sjogren's Syndrome (SS):

Oral cholinergic agonists/secretagogues:

- pilocarpine tablets 5mg bid-qid (i.e. Salagen®)
  - Non-selective muscarinic agonist
  - More side effects
  - Less expensive
- cevimeline 30 mg tid-tid (i.e. Evoxac®)
  - Selective muscarinic agonist
  - Less side effects
  - More expensive

*Small randomized studies suggest that these drugs decrease ocular signs and symptoms of dryness

(Tsifetaki et al 2003; Ono et. al 2004)

DRY EYE AND SYSTEMIC DISEASE: Sjogren's Syndrome (SS):

DRY MOUTH MANAGEMENT:

- Stimulate saliva production with sugar-free candy (xylitol), gum, dry mouth lozenges etc.
- Avoid mouthwashes with alcohol
- Prescription toothpastes
- Fluorinated floss
- Sip water constantly
- Stop smoking
- Artificial saliva (i.e. Numoisyn™ Rx)

TEST TIME…….

Which of these conditions are Sjogren's patients at more risk to develop?

A. Leukemia
B. Lymphoma
C. Diabetes
D. Hypertension

- 16 fold greater risk than normal population

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1798190/

DRY EYE AND SYSTEMIC DISEASE: Sjogren's Syndrome (SS):

- Cumulative risk of developing lymphoma:
  - 3.4% in first 5 years
  - 9.8% at 15 years
- Risk increases with time
- 1 in 5 patients with SS will die from lymphoma
  - **Early detection is the key!**
  - **Ask about chronic swelling and nodules**

Solans-Laque R, et. all. 2011; Loinnidis et al, 2002

DRY EYE AND SYSTEMIC DISEASE: Sjogren's Syndrome (SS):

MEDICAL MANAGEMENT:

- Refer for other associated symptoms:
  - PCP (monitor blood work for lymphoma etc.)
  - Dentistry (dry mouth, cavities, sores)
  - Gynecology (dryness)
  - Gastroenterologist (digestion, reflux)
  - Dermatology (dryness)
  - Neurology (depression, neuropathy)
  - Psychology (depression)
  - Rheumatology (RA, thyroid, SLE)

DRY EYE AND SYSTEMIC DISEASE: Connective Tissue & Collagen Vascular Diseases

Connective Tissue Diseases:

A. Inherited:
- Not necessarily associated with DED
  - Marfan syndrome; Ehlers Danlos syndrome

B. Autoimmune:
- Often associated with DED
- Specific antibody findings in blood work
  - Systemic Lupus Erythematosus (SLE) *
  - Rheumatoid Arthritis *
  - Scleroderma/systemic sclerosis, CREST syndrome
  - Polymyositis; Dermatomyositis
  - Juvenile arthritis

DRY EYE AND SYSTEMIC DISEASE:
Connective Tissue & Collagen Vascular Diseases

Rheumatoid Arthritis (RA): Definition

Chronic autoimmune disease characterized by symmetrical and destructive joint inflammation.

Can affect other body organs including the skin, lungs, eyes and blood vessels.

http://www.regenexx.com/

DRY EYE AND SYSTEMIC DISEASE:
Connective Tissue & Collagen Vascular Diseases

Rheumatoid Arthritis (RA): Epidemiology

- 0.8% of general population
- Women 3X men
- All races
- More common 4th,5th decades
- Genetic predisposition: 4x more likely if 1st degree relative
- 80% are RF (+)
- Frequently associated with Sjogren syndrome

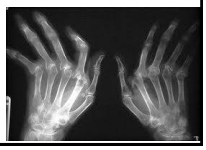
http://arcphysicaltherapy.com/

DRY EYE AND SYSTEMIC DISEASE:
Connective Tissue & Collagen Vascular Diseases

Rheumatoid Arthritis (RA) and Dry Eye:

- Most common ophthalmic manifestation
- Symptoms correlate with RA severity
- Decreased aqueous production is likely due to systemic inflammation or side effects of medications
- One study* showed: *Piper H, et. al. 2007.
  - >70% of subjects with RA had DED
  - ***ONLY 12% were being treated***

Why the disconnect?



DRY EYE AND SYSTEMIC DISEASE:
Connective Tissue & Collagen Vascular Diseases

1. Patients with significant systemic pain and discomfort often overlook ocular symptoms

2. We probably aren't asking the right questions:
   - Do you ask all RA patients about dry eye and variable vision?
   - Do you specifically test for dry eye in these patients?
   - Would it be appropriate to schedule a medically-oriented dry eye visit after their annual exam?

DRY EYE AND SYSTEMIC DISEASE:
Connective Tissue & Collagen Vascular Diseases

Systemic Lupus Erythematosus: Definition

Chronic inflammatory autoimmune disease that can attack many multiple body systems including:

- **Joints** (aches, arthritis, fatigue, fever)
- **Kidneys** (nephritis, edema)
- **Blood cells** (anemia, abnormal clotting)
- **Brain** (neurological changes, headaches)
- **Heart** (chest pain)
- **Lungs** (coughing, chest pain)
- **Skin and mucous membranes** (rashes, photosensitivity, ulcers, hair loss, Raynaud's phenomenon)

DRY EYE AND SYSTEMIC DISEASE:
Connective Tissue & Collagen Vascular Diseases

Systemic Lupus Erythematosus: Definition

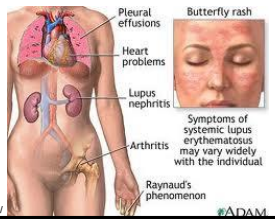
Diagnosed by symptoms and blood work:

- 97% are ANA (+)
- 50% have antibodies to double-strand DNA (anti-dsDNA)
- 30% have antibodies Smith proteins (anti-Sm)
- 30% have antibodies to phospholipid (anti-aPLs)
- 20% will have a false positive syphilis blood test
- May have antibodies to ribonucleoproetins (anit RNPs)
- May have antibodies to Ro/SS-A and La/SS-B

DRY EYE AND SYSTEMIC DISEASE:
Connective Tissue & Collagen Vascular Diseases

Systemic Lupus Erythematosus: Epidemiology

- Women > Men (9:1)
- African American/Asians > Caucasians
- Peak age (15-40)
- Most cases are sporadic (i.e. not inherited)



http://health.allrefer.com/

DRY EYE AND SYSTEMIC DISEASE:
Connective Tissue & Collagen Vascular Diseases

Systemic Lupus Erythematosus and Dry Eye:

- Small study* showed dry eye to be common in SLE:
  - DE was the most frequent ocular complaint (56%)
  - 57% of all subjects had pathological Schirmer score
- DED in SLE likely due to:
  - System-wide inflammation reducing aqueous production
  - Side-effects of multiple medications

*Ostanek L, 2007

DRY EYE AND SYSTEMIC DISEASE:
Connective Tissue & Collagen Vascular Diseases

DRY EYE MANAGEMENT (RA and SLE):

- **Control inflammation:**
  - Acute: Corticosteroid pulse therapy during flare-ups
  - Chronic: Topical Cyclosporine
- **Lubricate** (drops, gels, ung, inserts)
  - Punctal occlusion if inflammation is controlled
- Modify environment and diet
- Manage secondary ocular complications (i.e. uveitis)
- Close relationship with rheumatologist

DRY EYE AND SYSTEMIC DISEASE:
Connective Tissue & Collagen Vascular Diseases

CREST: Definition

C = Sub-epidermal calcinosis
R = Raynaud's syndrome
E = Esophageal dysfunction
S = Sclerosis
T = Telangiectasias

*only 2/5 required for a dx of CREST

DRY EYE AND SYSTEMIC DISEASE:
Connective Tissue & Collagen Vascular Diseases

CREST: Epidemiology

- Women>Men (4.6:1)
- AA > Caucasian
- Onset: age 30-65
- (+) Anti-centromere antibody, IgG (80-90%)
  - Sjo Test
- Exposure to certain toxic substances can trigger those genetically pre-disposed.

DRY EYE AND SYSTEMIC DISEASE:
Connective Tissue & Collagen Vascular Diseases

CASE:

DRY EYE AND SYSTEMIC DISEASE: Sarcoidosis

SARCOIDOSIS: Definition

- Chronic inflammatory disease where:
  - Clusters of immune cells (granulomas) form in organs
  - (+) Angiotensin-Converting Enzyme (ACE) in 50-80%
- Multiple organs/tissues can be affected:
  - Lymph nodes (90%)
  - Lungs (90%)
  - Liver (50-80%)
  - Joints (33%)
  - Eyes (25-80%)
  - Heart (10-25%)
  - Skin (25%)
  - Brain (5-25%)

http://www.nejm.org/doi/full/10.1056/NEJMra071714

DRY EYE AND SYSTEMIC DISEASE: Sarcoidosis

SARCOIDOSIS: Epidemiology

- Adults 20-40 years
- Affect all races but higher in AA and Northern European Whites
- Female > Male
- 5-fold increase if 1st degree relative
- 2/3 go into remission within 10 years; 5% pass away

http://www.nejm.org/doi/full/10.1056/NEJMra071714

DRY EYE AND SYSTEMIC DISEASE: Sarcoidosis

SARCOIDOSIS and DRY EYE:

- Lacrimal gland involvement occurs in 25-28%
  - Painless, bilateral, swelling (dacryoadenitis)
  - Due to granuloma formation in lacrimal gland
  - Moderate to severe K. Sicca

Treatment:
- Systemic steroids
- Methotrexate
- Hydroxychloroquine
- *Often, no systemic tx requ'd

http://escholarship.org/uc/item/80j4r407

DRY EYE AND SYSTEMIC DISEASE: Thyroid Dysfunction

Thyroid Dysfunction: Definition

- Imbalance of thyroid hormone due to dysfunction of:
  - Thyroid gland itself
  - Pituitary gland (secretes TSH to regulate the thyroid)
  - Hypothalamus (secretes TRH to regulate the pit. gland)
- Can effect heart rate, body temperature, protein production, lipid metabolism and alertness

DRY EYE AND SYSTEMIC DISEASE:
Thyroid Dysfunction

Thyroid Dysfunction: Epidemiology

- Affects 6-10% of Americans/Canadians
- Up to 50% undiagnosed
- Females > Males (8:1)
- Risk increases with age
- Dry eye can occur in BOTH hyper and hypo forms

National Women's Health Information Center Health Care Webpage; Gharib et., al 2004)

DRY EYE AND SYSTEMIC DISEASE:
Thyroid Dysfunction

Hypothyroidism:

- 2nd most common endocrine disorder
- Lethargy, weakness, dry skin, slow speech, cold intolerance, constipation, high cholesterol
- Most common autoimmune disease in patients with Sjogren syndrome.

Jara LJ et. al. 2007

DRY EYE AND SYSTEMIC DISEASE:
Thyroid Dysfunction

Hypothyroidism and Dry Eye:

- Lacrimal gland is a target receptor for thyroid hormone
- Chronic low TH = biochemical/structural changes
  - Decreased tear production

(Dias AK, 2007)

DRY EYE AND SYSTEMIC DISEASE:
Thyroid Dysfunction

Hyperthyroidism

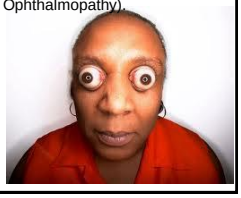
- Overproduction of TH
- Nervousness, weight loss, irregular heart rate, insomnia, hair loss, moist skin, fatigue, tremor, infertility
- **Grave's Disease** is 1 type of hyperthyroidism (1/500)
  - Body produces an "imposter" protein that can activate thyrotropin receptors
  - 50% of those with Graves' Disease develop Grave's Ophthalmopathy

DRY EYE AND SYSTEMIC DISEASE:
Thyroid Dysfunction

Graves' Ophthalmopathy:

- Graves' ophthalmopathy can develop before or after the onset of hyperthyroidism
- Ophthalmopathy can even occur in the absence of hyperthyroidism! (Euthyroid Graves' Ophthalmopathy).
- Smokers and diabetics are more likely to develop ophthalmopathy

(Prabhakar et. al., 2003)



DRY EYE AND SYSTEMIC DISEASE:
Thyroid Dysfunction

DRY EYE MANAGEMENT:

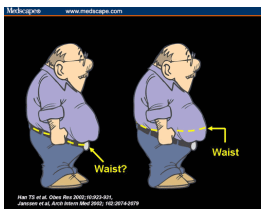
- Copious lubrication, gels, ointments, inserts
- Humidifier
- Moisture-chamber goggles
- Scleral lenses
- Cyclosporine ophthalmic emulsion
  - Not effective in exposure-related thyroid eye dz
- Co-management with Ophthalmology for complications resulting from compressive neuropathy

DRY EYE AND SYSTEMIC DISEASE:
DIABETES MELLITUS & METABOLIC SYNDROME

Diabetes Mellitus: Definition

A group of metabolic diseases characterized by hyperglycemia due to defects in insulin secretion, insulin activity or both.

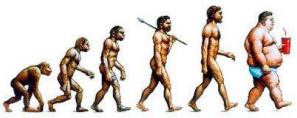
- Fasting plasma glucose of 100mg/dl
- Often associated with inactivity
- Associated with long-term damage, dysfunction and various organs.



DRY EYE AND SYSTEMIC DISEASE:
DIABETES MELLITUS & METABOLIC SYNDROME

Metabolic Syndrome: Definition

- Diabetes + any 2 of:
  - Abdominal obesity
  - Low HDL
  - High blood pressure
  - High triglycerides
- Increases with age
- Higher in Mexican Americans
- Increases risk of stroke and coronary heart disease



http://www.sourcewire.com/news/70084/

DRY EYE AND SYSTEMIC DISEASE: DIABETES MELLITUS & METABOLIC SYNDROME

Fast Facts:

- 26 million Americans/2.4million Canadians have Diabetes:
  - 20% undiagnosed
  - Expected to double in 2050
- Every 24 hours:
  - 4,100 new cases of DM
  - 55 new cases of blindness
- $174 billion in meds/testing equipment (USA)

(Centers for Disease Control and Prevention, 2011 and Dall TM, 2010)

DRY EYE AND SYSTEMIC DISEASE: DIABETES MELLITUS

Dry eye is one of the most common ocular manifestations of diabetes:

- >50% of diabetic patients have dry eye
  - 57% Type I
  - 70% Type 2
- Severity of retinopathy seems to be proportional to degree of tear film dysfunction.
- Non-proliferative DR patients had better tear films compared to patients with proliferative DR

(Seifart et. al.1994; Manaviat et. al., 2008; Wang, 2010, Yu et. al. 2008)

DRY EYE AND SYSTEMIC DISEASE: DIABETES MELLITUS

DIABETES MELLITUS and Dry Eye:

- Increase glucose in tear secretions ⇨ hyperosmolarity
- Corneal neuropathy ⇨ reduced aqueous secretion
- Pathological changes in the lacrimal gland ⇩ aqueous
- Increased prevalence of MGD (2x higher)

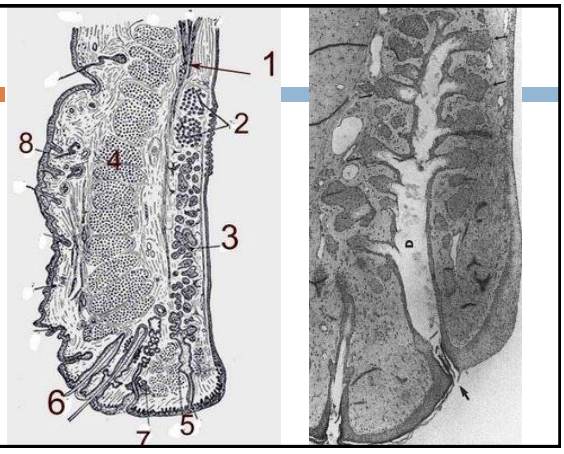
(Chous 2010; Benitez-Del-Castillo, 2007; Modulo, 2009, Ghasemi, 2008); Shamsheer 2015

Meibomian Gland Dysfunction:

"…a chronic, diffuse abnormality of the meibomian glands, commonly characterized by terminal duct obstruction and/or qualitative and quantitative changes in the glandular secretion. It may result in alteration of the tear film, eye irritation, clinically apparent inflammation, and ocular surface disease."

—The International Workshop on Meibomian Gland Dysfunction: Executive Summary

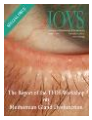
Nichols KK, et al. The international workshop on meibomian gland dysfunction: executive summary. *Invest Ophthalmol Vis Sci.* 2011;52(4):1922-1929.



The MGD Workshop Executive Summary (2011):

Prevelence has been estimated to be as high as 86% of all dry eye sufferers

"MGD may well be the leading cause of dry eye through out the world."

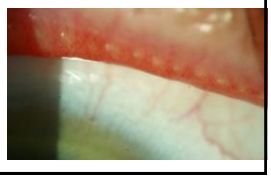


Clinical Assessment of MGD

Lid Margin Evaluation:

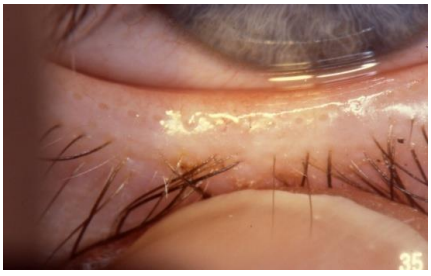
- Missing lashes?
- Increased thickness?
- Posterior lid margin redness?
- Telangiectasia?
- Scalloping/serration?
- Capped/distended MGs

Photo courtesy of Christine Tyler, OD



What if the lids and glands "look" normal?

MUST express to properly assess!



Clinical Assessment of MGD

Diagnostic expression should evaluate:

1. Ease of expression:
   - Mimic normal blink force
2. Secretion quality:
   - Thin and clear vs. turbid, thickened or none
3. Number of expressible glands

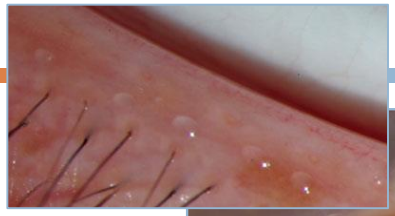
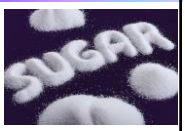


Image courtesy of Korb Associates

DRY EYE AND SYSTEMIC DISEASE: DIABETES MELLITUS

DRY EYE MANAGEMENT:



- Control of glycemic index!
- Attention to blepharitis and MGD:
  - Heat therapy, lid scrubs
  - Lid debridement (manual or BlephEx)
  - Gland expression (manual or Lipiflow)
  - Artificial tears with focus on restoring lipid layer
  - Cyclosporine; topical/oral macrolide; oral tetracycline
  - Omega 3 supplements
  - Autologous Serum (Schultze, 2006)

DRY EYE AND SYSTEMIC DISEASE:
Androgen Deficiencies

Androgen "Deficiencies"

- Hypopituitarism
- Adrenal insufficiency
- Ovarian insufficiency
- Glucocorticoid therapy
- Oral contraceptives
- Menopause
  - Androgens decrease by 50% in women by mid-40s

DRY EYE AND SYSTEMIC DISEASE:
Androgen Deficiencies

Androgen Deficiency and Dry Eye

- In the eye, androgens help maintain:
  - Lacrimal gland function
  - Meibum secretion
  - A non-inflamed state
- Estrogen-only HRT (Hormone Replacement Therapy)
  - Estrogen: reduces size, activity, and production of sebaceous glands.
  - 69% increase in dry eye compared to combined forms

Sullivan DA, 2003;

DRY EYE AND SYSTEMIC DISEASE:
Androgen Deficiencies

DRY EYE MANAGEMENT:

- Topical Testosterone/DHEA drops
- DHEA levels correlate positively with tear function in postmenopausal women
- Anecdotally beneficial in certain patients
  - No outcome studies to date
  - Must be compounded
  - No FDA approved

Mathers WD, 1998

DRY EYE AND SYSTEMIC DISEASE:
Dermatological Conditions

ROSACEA: Definition

- Chronic syndrome of the face, neck and scalp, characterized by flare ups and remissions
- Flushing, pimples, pustules, thickening, telangectasia
- Triggers:
  - Sun, heat, wind
  - Stress
  - Exercise
  - Alcohol

DRY EYE AND SYSTEMIC DISEASE:
Dermatological Conditions

ROSACEA: Epidemiology

- 1/20 people
- More frequent in northern European descent and those with fair skin
- Females > Males (3:1)
- Men tend to have more severe signs/symptoms

(Wilkin J et. al. 2002)

DRY EYE AND SYSTEMIC DISEASE:
Dermatological Conditions

ROSACEA and Dry Eye

- Ophthalmic rosacea occurs in 3-58%
  - Ocular signs occur prior to dermatological signs in 20% (kids!!)
- Signs and symptoms may include:
  - Lid inflammation, conjunctival injection, MGD
  - GRITTY SENSATION, burning, irritation
  - Recurrent hordeola or chalazia
  - Severe cases: corneal neovascularization, episcleritis

http://www.mrcophth.com/corneacommoncases/rosaceakeratitis.html

DRY EYE AND SYSTEMIC DISEASE:
Dermatological Conditions

PSORIASIS Definition:

- Chronic, inflammatory disease
- Hyperproliferation of keratinocytes in the epidermis
- Results in flaky, red, painful skin plaques

http://www.psoriasiswhat.com/

DRY EYE AND SYSTEMIC DISEASE:
Dermatological Conditions

PSORIASIS Epidemiology:

- 2% of the US population
- Female = Male
- Males: more severe presentations
- Onset:15-20 yr range, but can occur from birth
- ~20% have dry eye
  - Dry eye symptoms occur more in males

Langley RGB et. al, 2005

DRY EYE AND SYSTEMIC DISEASE:
Dermatological Conditions

DRY EYE MANAGEMENT:

- Dermatology referral
- Lid hygiene, including warm compress and scrubs
- Copious non-preserved artificial tears
- Topical corticosteroids for acute flares
- Topical ophthalmic cyclosporine
  - Reduce ocular inflammation
  - Improve tear production, if deficient

DRY EYE AND SYSTEMIC DISEASE:
Dermatological Conditions

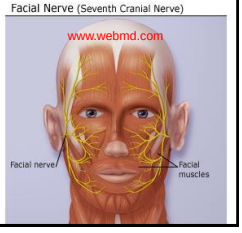
DRY EYE MANAGEMENT:

- Topical erythromycin or azithromycin
- Oral tetracyclines to modulate inflammatory pathways:
  - Decrease pro-inflammatory cytokines (IL-1 and TNF-alpha)
  - Inhibit matrix metalloproteinases -9 (MMP-9)
  - NO in pregnancy; NO under 8
  - Ex. 50mg doxycycline bid x 1 mo than qd x 2 mo
- May need systemic immunosuppression for psoriasis
- Omega 3 supplements (1-3 g/day)

DRY EYE AND SYSTEMIC DISEASE:
Bell's Palsy

BELL'S PALSY: Definition

- Temporary facial weakness or paralysis due to trauma of the facial nerve (cranial nerve VII)
- Commonly affects:
  - Facial Expressions
  - Blinking
  - Speech, Taste
  - Hearing
- Often resolves within 2 weeks to 3 months



DRY EYE AND SYSTEMIC DISEASE:
Bell's Palsy

BELL'S PALSY: Epidemiology

- 40,000 cases per year (USA)
- Females = Males
- Any age, but usually before 15 or after 60
- More common in diabetics or those with URI
  - May be linked to viral infection

www.nih.gov/disorders/bells

DRY EYE AND SYSTEMIC DISEASE: Bell's Palsy

DRY EYE MANAGEMENT

- Copious lubrication
- Gel or lid taping at night
- Removable lid weights
- Oral prednisone or acyclovir
  - May shorten course
- Scleral lenses

http://www.meddev-corp.com/

DRY EYE AND SYSTEMIC DISEASE: Inflammatory Bowel Disease

Inflammatory Bowel Disease: Definition

Chronic or recurring immune response and inflammation of the digestive tract.

- Ulcerative Colitis – affects the colon/large bowel
- Crohn Disease – can affect all parts of the intestines
  - Can also affect joints, eyes, skin and liver

***NOT Irritable Bowel Syndrome (IBS)

Centers for Disease Control and Prevention

DRY EYE AND SYSTEMIC DISEASE: Inflammatory Bowel Disease

Inflammatory Bowel Disease: Epidemiology

- 1.4 million people in the USA
  - Crohn Disease: Females> Males
  - Ulcerative Colitis: Males> Females
- Peak onset 15-30 years of age
- Caucasians > other races
- More common in smokers
- Strong genetic component
- May be associated with diet and/or meds, but unproven

DRY EYE AND SYSTEMIC DISEASE: Inflammatory Bowel Disease

Inflammatory Bowel Disease and Dry Eye

- 2:1 higher incidence of DED than normal population
- Dry eye in 42% of IBD
- Dry eye may be due to:
  - General inflammation
  - Vitamin A deficiency because of reduced intestinal absorption?

(Felekis T et. al 2009; Cury DB et. al. 2010)

DRY EYE AND SYSTEMIC DISEASE:
Inflammatory Bowel Disease

DRY EYE MANAGEMENT

- Close relationship with rheumatologist or GI specialist for systemic disease control
- Control ocular inflammation:
  - Acute: Corticosteroid pulse therapy during flare-ups
  - Chronic: Topical Cyclosporine
- Lubricate (drops, gels, ung)
- Modify environment and diet
- Manage secondary ocular complications (i.e. uveitis)

DRY EYE AND SYSTEMIC DISEASE:
CANCER, RADIATION and CHEMOTHERAPY

CHEMOTHERAPY:

- DES often occurs due to side effects of chemo medications, damage to goblet cells etc.

RADIATION:

- Damage to the lacrimal gland can occur following radiation treatment for head and neck cancers

DRY EYE AND SYSTEMIC DISEASE:
CANCER, RADIATION and CHEMOTHERAPY

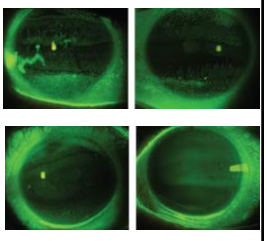
GRAFT VS. HOST DISEASE:

- Potential complication of bone marrow or stem cell transplant where transplanted cells attack recipient's cells
  - 30-40% chance if related
  - 60-80% chance if not related
- Ocular complications occur in 60-90%
- Severe OSD can occur, including corneal perforation

DRY EYE AND SYSTEMIC DISEASE:
CANCER, RADIATION and CHEMOTHERAPY

DRY EYE MANAGEMENT:

- No SCL wear during treatment
- Copious lubrication, inserts
- Occlusive eyewear
- Humidifier
- Punctal occlusion
- Scleral lenses for chronic conditions

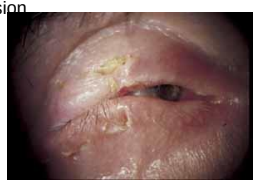


http://www.clspectrum.com/articleviewer.aspx?articleid=105794

DRY EYE AND SYSTEMIC DISEASE: CANCER, RADIATION and CHEMOTHERAPY

DRY EYE MANAGEMENT:

- Topical corticosteroid drops
- Cyclosporine ophthalmic emulsion
- Autologous serum
- Oral doxycycline, cevimeline, prednisone, cyclosporine
- Partial tarsorrhaphy



http://www.oculist.net/downaton502/prof/ebook/duanes/pages/v4/v4c020.html

DRY EYE AND SYSTEMIC DISEASE: Other causes……

ALCOHOLISM:

- Dehydration
- Present in tearfilm = hyperosmolarity = dry eye
- Severe alcoholics = malnutrition:
  - Vitamin A is important for tear production
    - 5,000 IU/day recommended
    - High doses can cause birth defects and death
    - Smokers taking beta carotene ↑ risk of lung cancer

DRY EYE AND SYSTEMIC DISEASE: Other causes……

FIBROMYALGIA:

- Dry eyes and mouth in 20–35% of patients

CHRONIC FATIGUE SYNDROME:

- Features of Sjogren's in 16% of patients
  - 2/3 satisfied diagnostic criteria for SS
  - Schirmer's test was abnormal in almost 60%

(Dinerman, 1986; Calabrese, 1994)

DRY EYE AND SYSTEMIC DISEASE: Other causes……

PARKINSON'S DISEASE:

- Progressive motor system disorder
- Loss of dopamine-producing brain cells
- Tremor, postural instability, rigidity, slowness
- **Low blink rate (1-2 per minute)**
- **Associated with seborrheic blepharitis**
- **Difficulty instilling drops**

DRY EYE AND SYSTEMIC DISEASE: Other causes……

MULTIPLE SCLEROSIS

Corneal neuropathy/impaired innervation

TREATMENT:

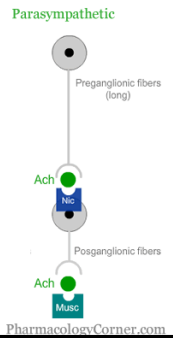
- Lubricants, bandage lenses, scleral lenses, punctal occlusion
- Collagenase inhibitors (i.e. tetracyclines)

Groos, E. *Cornea* 2004;94: 1189–1196.

PART III: MEDICATION AND DRY EYE

- Anticholinergics
- Diuretics
- Retinoids
- Botox
- Eye drops
- HRT/BCP
- Radiation
- Chemotherapy

Parasympathetic Nervous System



"REST and DIGEST" activities:
- •Salivation
- •Lacrimation
- •Urination
- •Digestion
- •Elimination

Anticholinergic activity decreases lacrimation

Drugs with Anticholinergic Activity:*

Antidepressants:
- Prozac
- Paxil
- Zoloft

Antipsychotics:
- Abilify
- Risperdal
- Haldol

Anxiolytics:
- Ativan, Valium
- Xanax

Antihypertensives:
- Beta blockers

Opioids:
- oxycodone
- hydrocodone

Antihistamines/decongestants:
- Clarinex
- Benadryl, Zyrtec (OTC)
- Tylenol/Advil PM (OTC)
- Sudafed (OTC)

Cough suppressants:
- Robitussen (OTC)
- Delsym (OTC)

Antispasmotics

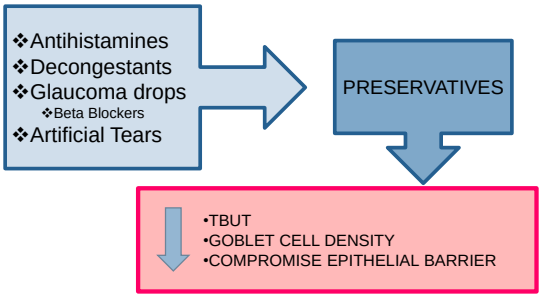
Incontenence
- Detrol

*Not all-inclusive

Other Drugs and Dry Eye

- Diuretics:
  - Treats HTN by causing kidneys to pull more water from the blood = dehydration = dry eye
  - ex. Aldactone, Lasix
- Retinoids:
  - Isotretenoin (Accutane)
  - Any history of use
- Botox
  - Blink dysfunction
  - Lagophthalmous
  - Ectropion

Drops and Dry Eye



PART IV JUVENILE DISEASES:

- Juvenile Diabetes (Type I)
- Juvenile Arthritis

DRY EYE AND SYSTEMIC DISEASE CONSIDERATIONS IN PEDIATRICS:

JUVENILE DIABETES (TYPE 1): Definition

- Immune system destroys insulin cells (beta cells) of the pancreas resulting in hyperglycemia.
- Due to genetics and environmental factors, not diet

DRY EYE AND SYSTEMIC DISEASE CONSIDERATIONS IN PEDIATRICS:

JUVENILE DIABETES (TYPE 1): Epidemiology

- 15,000 children are diagnosed per year in USA
- Non-hispanic caucasians most at risk
- No sex predilection
- Peak age of onset ~ 10 years of age (but can occur in any age, even adults)

www.diabetes.org

DRY EYE AND SYSTEMIC DISEASE CONSIDERATIONS IN PEDIATRICS:

JUVENILE ARTHRITIS: Definition

- Painful, swollen, stiff joint(s) > 6 weeks <16 yrs old
- May or may not have positive blood work:
  - (+) ANA = ⇧ likelihood of eye involvement (i.e. uveitis)
- Pauciarticular (≤ 4 joints; 75% ANA(+))
- Polyarticular (≥ 5 joints….often 20+)
- Systemic (fever, rash, many joints, death possible)

DRY EYE AND SYSTEMIC DISEASE CONSIDERATIONS IN PEDIATRICS:

JUVENILE ARTHRITIS: Epidemiology

- One of the MOST COMMON childhood diseases in USA
- ~300,000 children <18 yrs
- Girls> Boys, except for systemic JA (no sex predilection)
- Peak age of onset: 2-3 years

Lawrence RC et. al. 2998; Sacks J 2004

DRY EYE AND SYSTEMIC DISEASE CONSIDERATIONS IN PEDIATRICS:

CASE:

DRY EYE AND SYSTEMIC DISEASE CONSIDERATIONS IN PEDIATRICS:

PEDIATRIC SYSTEMIC DISEASE AND DRY EYE

Approximately 1.5% of healthy children have dry eye complaints compared to:

- 15% in Type 1 DM
- 11% in Juvenile Arthritis
  - Uveitis common and ASYMPTOMATIC
  - 30-40% severe vision loss

DRY EYE AND SYSTEMIC CONSIDERATIONS IN PEDIATRICS:

Dry eye in childhood is a potential indicator of systemic disease and may warrant a medical work-up, or at the least, a thorough Review of Systems

WRAPPING UP…….

- The most prevalent systemic diseases have significant associations with Dry Eye Disease.
  - Screen early
  - Treat aggressively
  - INFORM patients!
- Control of systemic disease is very important for DED management.

WRAPPING UP…….

Choose therapy based on causative nature:

- **Inflammation**
  - Topical steroids
  - Ophthalmic cyclosporine
- **Aqueous Deficiency**
  - Copious lubricants, gels, goggles, scleral lenses
  - Ophthalmic cyclosporine
  - Punctal occlusion if inflammation is controlled
  - Autologous serum
- **Meibomian Gland Dysfunction**
  - Lid therapy, lid hygiene and gland expression
  - Oil-based lubricants
  - Topical macrolides; oral tetracyclines
  - Omega 3 supplement/diet

WRAPPING UP…….

As optometrists, we have a unique opportunity to aid in the diagnosis of systemic disease and substantially improve our patient's quality of life through early intervention and appropriate dry eye therapy

The ABC's of Pediatric Eye Care

Dr. Kathleen Foster Elliott
918-388-3949

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INTRODUCTION

ABCs

A: AMBLYOPIA

B:BINOCULAR THERAPIES

C:CASE REPORTS

Pediatric Vision Television Clip

AMBLYOPIA

DEFINITION:

a condition that occurs when the vision of one eye is significantly better than the other eye and the brain begins to rely upon the better eye and ignore the weaker one.

STATISTICS

Amblyopia affects approximately 4% of the population

IT IS THE NUMBER ONE CAUSE OF MONOCULAR VISION LOSS IN CHILDREN

Amblyopia &Occlusion Therapy

Amblyopia is clinically diagnosed when one eye is 1.5 diopters different than the other eye

Options of Occlusion Therapy (Patching)

OCCLUSION THERAPY

1. Academic versus clinical differences

2. Hard patching for moderate -severe amblyopia(20/60 or worse)then taper

3. Clinical guidelines for patching

Binocular Therapy

1. Glasses

2. Vision Therapy for Convergence Insufficiency

GLASSES

1.Bilateral deprivational amblopia :very common with high astigmats,Hispanic/Latino and Native American population

2. Many times, these kids are 20/30- in the pediatrician or school screening office because of incredible accommodative ability of children's ciliary muscle

3.Vital to use 1% cyclopentolate ,wait 30 minutes , then retinoscopic evaluation

GLASSES

1. Proper adjustment of glasses imperative

2.children have flat bridged noses until older, consider : Solo Bambini;Miraflex frame design or silicone saddle bridge nosepiece

3.Custom Down's Syndrome(Trisomy 21)glasses

Vision Therapy (C.I.)

1. Convergence Insufficiency Exotropic Patient

2. Diagnosed with NPC,Low Amplitudes, greater XT at near ,and sometimes inadequate Stereo

3.

Vision Therapy

1.CITT: Convergence Insufficiency Treatment Trial

2. 12 week study jointly by NIH, NEI, Ophthalmologists, and Optometrists

3. Conclusions of study

4. Home or In Office Therapy Option

CASE REPORTS

1. NASOLACRIMAL DUCT OBSTRUCTION

2. SBS: SHAKEN BABY SYNDROME

3.DRUSEN/OPTIC NERVE EDEMA

N-L DUCT OBSTRUCTION

A 4 month old reports with symptoms of OD wet mattered eye x 6 wks,non responsive to topical antibiotic ung prescribed by pediatrician

1. a blockage is detected

2.tx options:in office procedure vs. general anethesia hospital treatment(video)

3.Post -Op care

Shaken Baby Syndrome

An infant patient is brought in by DHS case worker with sudden loss of vision bilaterally after being shaken vigorously by an adult care giver.No outward signs of abuse evident.

Q/A

1. What ocular (retinal) signs and symptoms would you expect to view with the BIO?

SBS

2.What would your work up include? Referral guidelines?

3.What guidelines/educational resources for SBS could be incorporated in your treatment/management for this case?

SBS

1.Ethical responsibility in SBS

2.Increased incidence in State of Oklahoma:Statistics

3.Attorney Input

Drusen vs Optic Nerve Edema

A 7 yo female presents with HA 2ce /wk,no ataxia, no N/V,no diplopia. VA 20/20 unilaterally and bilaterally.VF:normal (FFC OU).+1.00 OU cycloplegic refraction. Upon dilation, 78 D lens reveals 2+ elevation of both optic nerves, more pronounced temporally.

Drusen vs. Edema

1. Work up should include:

ULTRASOUND (B-Scan)

Drusen v. Edema

What if Ultrasound indicates Edema vs. drusen?

What tests?

MRI

Lumbar Puncture

MRI always FIRST

Conclusion

Q/A

Discussion of Clinical Findings

New Ideas in Glaucoma Management

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Missouri Eye Associates
McGreal Educational Institute

Excellence in Optometric Education

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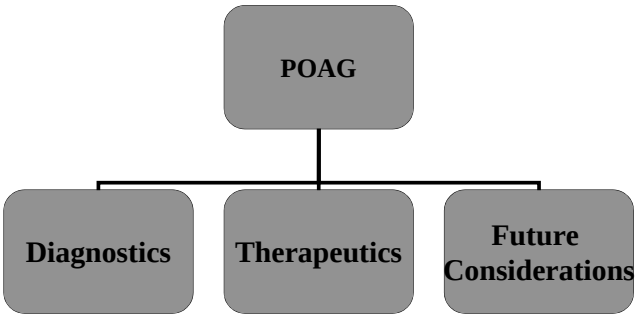
JAM

Glaucoma Evolution



Glaucoma Evaluation is Transforming

- In the past, detection & management relied on functional assessment
  - Visual fields (white-on-white)
    - Insensititve for detecting early POAG
    - High degree of variability
- Recently, structural change over time longitudinal studies have validated the role of structural imaging
  - Are structural defects with normal functional tests false positives or POAG?

JAM

Glaucoma Evaluation is Transforming

- Glaucoma considered a NOCTURNAL disease
- IOP increases starting at bedtime and stay high all night
- Concept of “flattening the curve” of IOP
- New emphasis on sleep apnea link to POAG
  - Blood flow issues
  - Sleep lab studies
- Ocular blood flow
  - Systemic medications worsen blood flow to head
  - CMS temporary code for measuring ocular blood flow

JAM

24 Hour Contact Lens Sensor

- Weinreib, Mansouri, Romenet
- Accurate and reproducible method to measure nyctohemeral IOP rhythm
- “Triggerfish”
- Significant rhythm detected
- Nocturnal disease nature of glaucoma
  - Highest IOP at 4 am
- Sleep lab studies in Obstructive sleep apnea
- Consider especially in low tension glaucoma

Triggerfish / Sensimed, Switzerland

- Received FDA approval for 24 hr metrics to assess IOP, peak IOP, fluxuation, and allow customized timing of drop application (chronotherapy, IOP modulation)
- Measures change of corneo-scleral not IOP in mmHg
  - Correlates well with IOP
  - CLS output may reflect changes that are more relevant to glaucoma damage than pure IOP
- Single use CL records 300 data points for 30 seconds at 5 min intervals transmitting them wirelessly to antenna worn around eye, then onto a recorder around neck

Gonioscopy 92020

- Bilateral
- Requires documentation
  - describe visible angle structures
- No limitations to diagnostic groups in most states
- Fee $25.71-

JAM

Pachymetry 76514

- Bilateral
- Measurement of central corneal thickness (CCT) proven by Ocular Hypertension Treatment Study (OHTS) to be standard of care in diagnosis and management of glaucoma, glaucoma suspect and ocular hypertension
- Also billable for keratoconus, corneal transplants, cataracts with corneal dystrophies, guttata, edema
- Requires Interpretation & Report
- Fee $11.92

JAM

Pachymetry

- Risk of POAG conversion in OCHTN is 11% (OHTS) in 5 years
- Risk is greater if CCT is THIN
  - 36%
  - Thin is <555um
- Thin corneas are an independent risk factor in OCHTN
- Thin corneas have not yet been found to be an independent risk factor for POAG

JAM

Pachymetry

- IOP correction by correlation to corneal thickness is NOT POSSIBLE!
  - A linear relationship does not exist!
  - Careful examination of regression analysis (scatter graph of IOP relative to CCT) demonstrates huge bandwidth
- Adjusting IOP by CCT instills a degree of accuracy into an inaccurate measurement
- It is possible to adjust the IOP in the WRONG direction
- Barbados study of black patients shows no correlation of CCT/IOP
- "Trying to be more precise than this is not supported by the data and may be harmful to patient care" Jamie Brandt, MD Dir Glauc Src, UCD / OHTS investigator

JAM

Serial Tonometry 92100

- Bilateral
- Requires Interpretation & Report
  - Example: Angle closure glaucoma
  - multiple measurements over time
- Fee $55.91-

JAM

IOP Measurements By DCT After LASIK

- "Corneal ablation of 90.0 +/- 49.18u reduced IOP as measured by GAT by 3.0mm... no significant change in IOP was recorded by DCT (-0.2MM)"
- Clinically validated by manometric studies of true intracameral pressure
- LASIK case volume in US is 7,401,400
  - GAT DOES NOT WORK!

Kaufmann C, et al IOVS 2003; 44:9:3790-3794

Corneal Compensated IOP (IOPcc)

- 7CR Autotonometer – Reichert
- Pressure significantly less affected by the cornea than other instruments
  - Hysteresis is a risk factor for glaucoma
- Incorporates bidirectional applanation technology used in ORA, to quantify biomechanical properties of cornea
- Non contact (air puff) simultaneously provides a Goldmann-correlated (IOPg) and IOPcc
- Helpful in patients with cornea disease and glaucoma

Corneal Hysteresis 92145

- Unilateral or Bilateral
- Corneal hysteresis determination by air impulse stimulation
- Requires Interpretation & Report
- Fee $ 15.37

JAM

i-Care Tonometer

- Hand held, portable
- NO ANESTHESIA
- Disposable probe
- Accurate
- Power – AA batteries
- Measurement in 0.1 sec
  - Measures motion of cornea
- Digital display
- Memory – last 10 results

i-Care Tonometer

- Applications
  - Eye MDs
  - ODs
  - General practitioners
  - Pharmacy
    - Screenings
  - Veterinarians
  - Consumers
    - Self screenings

Glaucoma Pipeline

- Extracellular Matrix metalloproteinases
- Oral neuroprotectants - Memantine (Nameda)
- Sustained release formulations
  - Punctal plugs
  - Injectable implants
- Home IOP monitors – 24 hr monitoring
  - Mansouri & Weinreib used telemetric contact lens sensor
  - IOP doesn't behave the same in individuals right/left eye
    - Monocular therapeutic trials have been invalidated
  - IOP not conserved from day to day

Glaucoma Pipeline

- Combined structure-function index (CSFI) – new paradigm
  - Unlike VF testing alone, performs well in detecting pre-perimetric glaucoma
  - Unlike imaging alone, successful at discriminating early vs moderate and moderate vs advanced glaucomatous damage
  - Reported as a % of loss of ganglion cells
  - Detects progression better than other indicies
    - CSF I= 22%, VFs = 8.5%, OCT = 14.6

Glaucoma as a Two Pressure Disease

- Intracranial space and intraocular space are two fluid filled compartments separated by the lamina cribrosa
  - If pressure on one side (IOP) matters than why wouldn't pressure on the other matter?
  - CSF pressure begins to drop after age 40-50, same time when glaucoma prevalence increases
  - ICP lower in patients with normal tension glaucoma & high tension glaucoma compared to normal
  - ICP is lower in normal tension vs high tension glaucoma
  - Theory is laminar deformation caused by translaminar pressure difference of IOP & ICP
    - Squeezes axons of RGC's as they travel through nerve
    - Disrupts axonal transport leading to cell death
- Glaucoma is multifactorial and IOP is only one factor

Glaucoma Pipeline

- Intracranial cerebrospinal fluid pressure (CSF-P) is lower in glaucoma
- Trans-laminar pressure difference (TLPD)
  - TLPD = IOP – CSFP (normal is 4-8mmHg)
  - Lumbar measurements not as accurate as orbital CSF-P
  - MRI offers high resolution of optic nerve diameter (OND) and sheath diameter (ONSD) and optic nerve subarachnoid space width (ONSASDW)
    - Is a reliable predictor of CSF pressure

Evolving Views on IOP

- IOP is a causal risk factor in development of glaucoma at all levels of IOP
- IOP plays a role in every eye with glaucoma
- Knowledge of IOP is not necessary to diagnose or detect progression in glaucoma
- What aspects of IOP behavior is most responsible for glaucoma progression?
  - Mean IOP/ Peak IOP/ we don't know!
- Home tonometry is coming into practice and will help identify patterns of IOP
- Ocular perfusion pressure (OPP) is a risk factor for development of glaucoma (low OPP)
  - Difference between systemic BP & IOP

Visual Field 9208x

- Bilateral
- Requires Interpretation
  - separate report form
  - narrative in body of medical record, on date of service
- Fee $43.88- (-81) $57.37+ (-82) $65.92- (-83)

JAM

FDT Perimetry Abnormalities as Predictors of Glaucomatous VF Loss

- 105 eyes of 105 glaucoma suspects
  - IOP 23mm+ or disc damage on photos
  - SAP VF normal
- Baseline FDT obtained
- Mean follow-up 41 months

Medeiros FA, et al AJO 137:863-871, 2004

FDT as Predictor of VF Loss

- 16% (17 pats.) converted on SAP VF
- In pats. with abnl. FDT at baseline:
  - Probability of developing abnl. SAP:
  - 30%
- Pats. With NL FDT at baseline:
  - Probability of developing abnl. SAP:
  - 4%

Other Important VF Studies

- Paczka (2001) - found FDT better overall performance in detecting damage than RNFL photographs
- Kondo (1998), Wu (2001) - In patients with SAP VFDs restricted to 1 hemifield, FDT has shown to be able to detect functional losses in the other hemifield
- Medeiros (2004) – functional defects in FDT predict future defects on SAP

Other Important VF Studies

- Kim (2007/AAO) – when SAP is normal, some patients with VFD detected by FDT showed decreased NFL thickness (OCT)
  - Provide evidence that coincident FDT & OCT abnormalities may be an early sign of glaucoma

Visual Field Testing for Specific Functions

- Short wavelength autoperimetry (SWAP)
  - Bistratified ganglion cell (9%) short-wavelength cones
- Frequency doubling technology (FDT)
  - Magnocellular ganglion cells
- Motion automated perimetry (MAP)
  - Magnocellular ganglion cells (3%)
- High pass resolution perimetry (HPRP)
  - Parvocellular ganglion cells

Closing Statements on Perimetry

- Advances in perimetry are continuing
  - Faster third generation algorithms reduce test time by 50%
- Customization for specific needs
  - Early detection / established glaucoma / screening
- Early VF loss is often selective, with specific types of axons disturbed
  - SWAP allows early recognition, HPRP follows progression
- SAP perimetry will continue to be preferred for established glaucoma with VFDs
  - Considerably improved methods of computer-assisted interpretations of serial VFs
- Screening methods will sacrifice sensitivity for specificity and ease of use to detect the half of glaucoma patients who have undiagnosed disease
  - Deployed in non-professional environments

Prognostic Factors in VF Progression

- Ophth 2013;120:512-519 Ernst, et al, in order
- Age (for all OAG)
- Disc hemorrhages (for NTG)
- Baseline VF loss
- Baseline IOP
- Exfoliation syndrome
- CCT
- Peri-papillary atrophy (for NTG)
- Proven previous VF progression

Glaucoma & the Brain

- Researchers view Glaucoma as a disease of the brain
  - Neurodegenerative disease
- Glaucoma shares common features with AD, Parkinson's and Lou Gehrig's diseases
- Offers potential for new treatments that promote nerve health, neurotrophic factors which can help at multiple places in the visual pathway
  - Neuroprotection – Ciliary neurotrophic factor (CNTF)
  - Neuroregeneration – increase axon regrowth
  - Neuroenhancement – improve support between dying RGC and surrounding cells in brain and retina

New Functional Testing

- Pattern ERG (PERG) – improves with decreased IOP
- Multifocal VEP – higher flicker VEP
- Isolated Check VEP
  - Tests central vision
  - Bright Check Pattern (M-cells)
  - Dark Check Pattern (off pathway cells)
- Pupil perimetry (True Field Analyzer)
  - Computer measures pupil (involuntary) diameter in response to retinal visual stimulation

JAM

Visual Evoked Potential

- Nova-DN VEP Vision Testing System (Diopsys)
  - Not new technology, but clinically useful and affordable is
    - Improves sensitivity & specificity in glaucoma diagnosis
  - Short duration transient VEOP (SD-tVEP) to record electrical responses of the entire visual system
  - Objective test, 4-6 minutes
  - Low contrast testing – health of magnocellular pathways
  - High contrast testing – health of parvocellular pathways
  - Serial tracking of disease progression
  - Useful in MS, TBI, Stroke and other CNS disorders

Visual Evoked Potential - Coding

- Nova-DN VEP Vision Testing System (Diopsys)
- CPT: 95930
  - Bilateral
  - No CCI bundling edits in office setting
- ICD – includes many optic nerve and retina disorders, visual disturbances (amblyopia, SVD, night blindness, sudden vision loss, et al), neurological (aphasia, MS, Lyme, TBI, intrcranial diseases, conversion, gait abn, coordination, etc
- Fee: $133.19 (range $60-$180 commercial)

FAF Background Information

- FAF imaging is in-vivo method for mapping of fluorophores in fundus
  - Naturally occurring and pathological
- Dominant source are fluorophores like A2-E in lipofuscin granules
  - Accumulates in post mitotic RPE
  - By-product of incomplete degradation of photoreceptor outer segments
- RPE captured by FAF lies just above choroid
  - Not captured by photography or FA photography

JAM

FAF Background Information

- Two filters required
  - One in conjunction with flash
    - Excites fluorescence of RPE/Bruch's
  - Barrier – blocks all other wavelengths back to camera
- Any structure without fluorescence is BLACK
  - In pathology dead photoreceptor cells shed distal outer segments (POS) stacks for photoreceptor renewal
  - Dead cells trapped in RPE leave behind cell walls, lipid, blood
  - This debris is lipofuscin
- All others are SILVER

JAM

Scanning Computerized Ophthalmic Diagnostic Imaging 92133

- Unilateral
- Applies to glaucoma and retinal evaluations
  - Retinal Thickness Analyzer (RTA)
  - Heidelberg Retinal Topography (HRT3, Spectralis)
  - Zeiss Optical Coherence Tomography (GDX, Stratus/Cirrus OCT)
  - Optovue (RTVue, iVue)
- Requires Interpretation & report
- Fee $42.42

JAM

Scanning Computerized Ophthalmic Diagnostic Imaging 92133

- Unilateral or bilateral
- Applies to glaucoma or optic nerve evaluations
  - Heidelberg / Heidelberg Retinal Topography (HRT, Spectralis)
  - Carl Zeiss / Optical Coherence Tomography (GDX, Stratus, Cirrus)
  - Optovue / (RTVue, iVue)
  - Marco / Retinal Thickness Analyzer (RTA)
- Requires Interpretation & report
- Fee $42.24

JAM

Ophthalmic Genetics

- Researchers have identified genes for OAG
  - TIGR/Myocilin = juvenile OAG
  - OPTN (optineurin) = Primary OAG (NTG)
    - Optineurin may provide neuroprotection to optic N
  - CYP1B1 = Congenital glaucoma
- Genetic testing will allow clinicians to determine if Pt is predisposed to or affected with specific type of glaucoma, even before symptoms appear
- OcuGene (InSite Vision/Alimeda) – simple, in office test, 99% accurate detection of TIGR (trabecular meshwork inducible glucocorticoid response gene)
  - Positives may be treated more aggressively, earlier

New Ideas in Glaucoma - Genetics

- Multiple genes & environmental factors interact in this heterogenous complex disorder
- Family history is one of the most important risk factors
- First degree relatives of affected patients demonstrate glaucoma 10 times more than general population
- 16 loci contributing susceptibility identified
  - Of these four genes isolated
  - Myocilin - more likely in early age of onset, family hx, elevated IOP
  - Optineurin
  - WDR36
  - NTF4

Low Tension Glaucoma

- Compromised ocular blood flow
- 50% have a cause / find it / fix it
  - Past hx transfusions, bleed, hypovolemic
  - Medications: B-blockers, digoxin, digitalis
  - MRI: orbits & brain
  - R/O all cardiovascular causes of LTG
    - CBC/anemias, CA doppler, TEE, sleep studies, coagulaopathies (PTT), overly fit (low BP)
- Treatment
  - Decrease IOP, avoid B blockers, start with PG, bromonidine, CAIs last resort
  - Ginko biloba 60mg/D: inc fluidity without affecting platelet aggregation

Characteristics of Glaucoma in Japanese Americans

- Pekmeezi M ArchOphthal 2009;127(2):167
- 1732 patients in Japanese-American clinic over a ten year period
  - 112 with glaucoma, 17% HTG, 70% NTG
- Proportion of patients with NTG was 4-fold higher than those with HTG

Do Superactivated Platelets Explain Disc Hemorrhages in Glaucoma?

- Disc Hemorrhage is a poor prognostic sign in ALL studies
- University of Chicago – SAPs associated with AD, TIA, corticle stroke
- Hemorrhages of optic nerve head and nailfold capillary bed characterize POAG
- Suggest that SAPs play a role in POAG
  - POAG patients display an elevated level of activated SAPs which are hyper coagulable

Do Superactivated Platelets Explain Disc Hemorrhages in Glaucoma?

- Platelets provide role in blood coagulation and circulate until they encounter thrombogenic elements and become activated, sometimes becoming superactivated
  - Phenotypically different and posses enhanced procoagulant and prothrombogenic activity
- Videocapillaroscopy to quantify vascular changes in the nailfold region demonstrated hemorrhages in 96.8% POAG, 92.3% LTG, secondary glaucoma 75%
  - 6 fold more hemorrhages than controls but different between all 3 forms of glaucoma (?)…new screening tool or ancillary

From the Literature

- 10% of blindness from glaucoma is from poor adherence to prescribed drugs
- DM, duration, fasting glucose, assoc w higher risk of POAG, and higher IOP – Di Zhao Ophthal 2015; 122
- Nocturnal hypotension predicted VF loss and worsening of defects – Charlson Ophthal 2014; 121
- Statin use significantly reduces risk of OAG in persons w hyperlipidemia – Stein Ophthal 2012; 119
- 3-5 times risk of acute angle closure with topiramate and buproprion
- GCC loss linked to decreased MPOD

Anti-Glaucoma Agents

- Non-Selective B-Adrenergic Antagonists
  - Timolol (Timoptic 0.25%, 0.50%, XE, Istalol/Ista Pharmaceuticals)
  - Levobunolol (Betagan 0.25%, 0.50%)
  - Metipranolol (Optipranolol 0.3%)
- Selective B-Adrenergic Antagonists
  - Betaxolol (Betoptic-S 0.25%, 0.50%)
  - Levobetaxolol (Betaxon)
  - Carteolol (Ocupress 1.0%)

Anti-Glaucoma Agents

- Prostaglandin Analogue
  - Latanoprost (Xalatan 0.005%) generic 3/2011
  - Bimatoprost (Lumigan 0.03%, Lumigan 0.01%*)
  - Travaprost (Travatan Z 0.004%) – No BAK
  - Tafluprost (Zioptan PF)
- The future – 7 PGA drugs currently being developed for sustained drug delivery systems
  - Nanoparticle size for injection

Latanoprost 0.005%

- Topical prostaglandin
- Indications: open angle glaucoma or ocular hypertension
- Side effects – hyperemia of conjunctiva, iris pigmentation/color change, lid erythema, eyelash growth
- Dosage: once daily at bedtime
- Advantages: monotherapy/compliance, favorable SE profile, longest track record, generic March 2011
- Available as ***Xalatan***
- ***Sustained release punctal plug coming soon!!***

Bimatoprost 0.03% & 0.01%**

- Topical prostaglandin
- Indications: open angle glaucoma or ocular hypertension
- Side effects – hyperemia of conjunctiva, iris pigmentation/color change, lid erythema, eyelash growth
- Dosage: once daily at bedtime
- Advantages: monotherapy/compliance, favorable SE profile with lower concentration but equal IOP lowering
  - Switch when having SE with other PGs or as first line PG
- Available as ***Lumigan, Lumigan 0.01%***
- ***Subconjunctival depo & external implant coming !!***

Bimatoprost 0.03% & 0.01%**

- ForSight Vision5 – Helios Insert
  - Polymer bimatoprost matrix in a soft compliant ring 26mm in diameter
  - Applied to ocular surface in office maintained under lids
  - Mean IOP reduction a t 6 months of 6.5mm
- Allergan – developing Bimatoprost SR
  - The amount of drug in implant is equivalent to one drop bimatoprost
  - Safer, less drug exposure, less side effects
  - Delivered intracamerally, prefilled single use applicator
  - Drug depleted in one year, implant gone in 2 years
  - POAG pts live 16 yrs / 32 injections / leave behind benign

Travoprost 0.004%

- Topical prostaglandin
- Indications: open angle glaucoma or ocular hypertension
- Side effects – hyperemia of conjunctiva, iris pigmentation/color change, lid erythema, eyelash growth
- Dosage: once daily at bedtime
- Advantages: monotherapy/compliance, favorable SE profile, long track record
- Available as ***Travatan-Z***
- ***Coming soon as medicated punctal plug***

Tafluprost 0.0015%

- Topical prostaglandin, first preservative-free preparation
- Indications: open angle glaucoma or ocular hypertension
- Supplied: 10 PF ampules per pouch, 3 pouches/box
- Side effects – same as other PGA
- Dosage: once daily at bedtime
- Storage: refrigeration necessary until pouch is opened, then once opened room temperature is fine
- Coming soon Tafluprost/timolol (Santen)
- Available as ***Zioptan / Merck***

Anti-Glaucoma Therapy

- Adrenergic Agonists
  - Dipivefrin (Propine 0.1%)
  - Epinephrine (Epinal,Eppy-N, Epifrin, Glaucon)
  - Apraclonidine (Iopidine 0.5%, 1.0%)
  - Brimonidine (Alphagan 0.2%, Alphagan P-0.1%, 0.15%) / Timolol (Combigan)
    - 41% less ocular allergy with Alphagan P vs Alphagan over 12 months
    - Only ophthalmic glaucoma drug without BAK
- Cholinergic
  - Pilocarpine (Pilocar 0.50% - 8.0%, Pilogel 4%)
  - Carbachol (Carbachol 0.75%, 1.5%, 2.25%, 3%)
  - Echothiophate Iodide (0.03%, 0.06%, 0.125%, 0.25%)

Antiglaucoma - CAI

- Topical
  - Dorzolamide (Trusopt)
  - Dorzolamide-Timolol (Cosopt/Cosopt PF)
  - Brinzolamide (Azopt)
- Oral
  - Acetazolamide (Diamox)
  - Methazolamide (Neptazane, MZM)
  - Dichlorphenamide (Darinide)

What is the Next BIG THING?

- Latanoprostene bunod (Vesneo) by Valeant/B&L-Nicox
  - Novel nitric oxide donating prostaglandin F2a analog
  - Decreases IOP 7.5mm-9.1mm from baseline between weeks 2 &12 in phase 3 trials
  - Superior to timolol
  - Met endpoints both primary and secondary
  - Once daily dose

What is the Next BIG THING?

- (Rhopressa) by Aerie Pharma
- FIRST NEW MECHANISM OF ACTION in 20 years
- Triple action
- Inhibits rho kinase (ROCK) & norepinephrine transporter (NET), both biochemical targets for lowering IOP and reduces episcleral venous pressure (EVP) by 35%
  - ROCK inhibitors increase outflow via TM which is 80% of drainage from eye
  - NET inhibitors reduces production of aqueous
- Once daily dose

What is the Next BIG THING?

- (Rhopressa) by Aerie Pharma
  - Downstream effect of small-G protein Rho
  - Potential to modify disease course by arresting fibrosis of TM
  - Suppresses activity of profibrotic proteins TGF-B2, CTGF on TM cells
  - Lowering EVP may help LTG or angle closure types
  - Theory – TM relies on aqueous percolation to supply nutrients, antioxidants
    - Diverting into uveoscleral outflow may not be good for TM long term health
- Mean IOP average reduction 6mm (?stand alone)

What is the Next BIG THING?

- (Roclatan) by Aerie Pharm
- Quadruple action – more impressive
  - Mean IOP 25.1 decrease to 16.5 on day 29
  - 2mm better than latanoprost alone
- Combination of triple action Rhopressa & Latanoprost
- Efficacy – superior to latanoprost
- Only glaucoma product covering full spectrum of currently known IOP lowering mechanisms of action
- Once daily dose
- SE - hyperemia

Glaucoma Market to Grow to $3B

- 2.3 Billion grows to 3 Billion by 2023
- Projected growth in seven major markets – US, France, Germany, Italy, Spain, UK and Japan is 2.4%
- Driven by first in class drugs
- Roclatan is forcast to achieve the highest sales expected to generate 262million in 2023
- Increase attributable to introduction of new drugs between 2013 and 2023 and overall increase in glaucoma prevalence
  - Mostly due to aging society in the US

Ranibizumab / Lucentis

- for injection
- Dose – 0.5mg/monthly
- Administration – 27g needle intravitreal injection
- Indication – neovascular “wet’ macular degeneration
- Contraindications – ocular infection
- Warnings – risk of endophthalmitis, increased IOP
- Dose – may decrease to q3m after 4 monthly injections
  - Less effective
- Studies – ANCHOR, SAILOR, PIER, MARINA, FOCUS

JAM

Bevacizumab / Avastin

- for injection, twice the half life of Lucentis, fraction cost for AMD
- Effect – Anti VEGF for CA of lung and colorectal CA
- Dose – 0.5mg/monthly
- Administration – 27g needle intravitreal injection
- Indication – neovascular "wet' macular degeneration
- Contraindications – ocular infection
- Warnings – risk of endophthalmitis, increased IOP
- Dose – may decrease to q3m after 4 monthly injections
  - Less effective

JAM

Avastin for EVERYTHING ocular

- AMD
- PDR
- PDR with vitreous hemorrhage
- DME
- Vein occlusions
- ROP
- Choroidal melanoma
- NVG
- The future is topical eyedrops, oral formulations

JAM

Surgical Glaucoma Therapy

- Argon Laser Trabeculoplasty (ALT, LTP)
- Selective Laser Trabeculoplasty (SLT)
  - Q switched Nd:YAG selectively targets pigmented trabecular cells (increasing activity?)
  - Increases immune system by increasing monocytes & macrophages in TM
  - Selective because it does not cause appreciable damage to TM
  - 50 confluent applications to 180 degrees @0.06mJ
    - No blanching or bubble phase needed
  - Addresses greatest roadblock = compliance with medical therapy

Angle Laser Surgery

- Wise – 1970
- Mechanism – not known but shrinkage of trabecular ring with widening of spaces and decreased resistence to outflow is probable
- Particularly effective (90% controlled after one year)
  - Psuedo-exfoliation (PXF)
  - Pigment dispersion syndrome (PDS)
  - POAG
- Slowly and constantly loses effect
  - 55% at 5 years
  - 30% at 10 years
- Low complications with spike in IOP 30% (post-op)

Surgical Glaucoma Therapy

- Argon Laser Trabeculoplasty (ALT, LTP)
  - Q switched Nd:YAG selectively targets pigmented trabecular cells (increasing activity?)
  - Increases immune system by increasing monocytes & macrophages in TM
  - Causes appreciable damage to TM
  - 85 confluent applications to 180 degrees @0.06mJ
    - Blanching or bubble phase needed to assure proper treatment
  - Addresses greatest roadblock = compliance with medical therapy
  - Usually performed over 180 degrees of TM
    - Can be repeated to the other 180 degrees later if needed

Laser Surgery Before Medical Therapy?

- Glaucoma Laser Trial (GLT)
  - Multicenter/randomized study of safety and efficacy of laser first for newly diagnosed glaucoma
  - IOP better controlled at 2 years and 7 years
    - Less deterioration of cupping
    - Less deterioration of visual field
  - Limitations
    - Temporary effect
    - Better topical drugs with low side effects

New Approach to SLT?

- SLT available >12 years
- IOP decreases as well as PGA without medications
  - Daily medical adherence & tolerability issues
  - Targets pigment cells of TM without damage to TM structures
  - Can be safely effectively repeated
- Standard therapy – 70 to 80 spots over 360 degrees
  - Starting at 0.5mJ titrating up to bubble
- Annual retreatment – 40 to 50 spots over 360 degrees
  - Starting at 0.4mJ, titrating up to bubble

New Approach to SLT?

- Results
  - 16% on topical Rxs in follow up vs 53% with SLT and 62% with ALT
- Conclusion
  - Annual SLT with lower power better then as needed SLT or ALT in reducing need for medications and time to medications in newly diagnosed glaucoma or ocular hypertension

New Ideas in Glaucoma

- Minimally Invasive Glaucoma Surgery (MIGS)
  - Micro-stents emerging from trials, recent FDA approvals
  - Studies (COMPASS/phase 3) showing limited efficacy of third IOP lowering agent
  - Makes argument for MIGS after failing with two topical Rxs
  - Safer but less effective than older bigger surgeries
  - Goal – MIST/minimally intrusive sustainable therapy not maximally tolerated medical therapy
- Glaukos iStent
- Solx Gold Implant
- AqueSys XEN Gel Stent

New Ideas in Glaucoma

- Minimally Invasive Glaucoma Surgery (MIGS)
  - Endocyclophotocoagulation (ECP) / Endo Optiks
  - iTrack catheter (iScience)
- Nocturnal hypotension – risk factor for glaucoma
  - Ambulatory 24 hour BP monitoring is rountine in clinical practice and can identify nocturnal dips in BP
  - Reduction in dose of blood pressure medications may be helpful
    - If PCP deems this inappropriate ingestion of salty snack like small bag of potato chips before bed may help prevent dips

Endocyclophotocoagulation -ECP

- Reduces production of aqueous fluid by utilizing laser energy to treat the ciliary processes
  - Disables some of the ciliary epithelium
    - Works on inflow production of aqueous
  - Ideal procedure to combine with cataract surgery
    - Endoscope can be inserted through same incision for cataract surgery
    - Expect 20-30% drop in IOP
    - Drop in IOP is not immediate like filtering surgery but improves with post operative decrease in inflammation
    - Requires viscoelastics out of the bag to move iris for probe

Trans-scleral Cyclophotocoagulation

- Historic methods of ciliary body destruction
  - Cyclocryopexy, etc
  - Many complications including cataract, pain, phthsis
  - Simple and in-office procedures
- Ab interno or Ab externo
- Non-contact or contact Nd:YAG, or Nd:Diode
- New Method – micropulsed laser uses 0.5us doses, rapidly alternated with 1.1us rest over 100 sec rather than for 2 sec continuously as previous
  - Can use earlier

Addressing Outflow - Goniotomy

- Kahook double Blade (New World Medical) – single use instrument excises a strip of trabecular meshwork
- Trab 360 (Site Sciences) – completes a 360 degree cut in TM using a filament inside schlemm's canal
- Trabectome (NeoMedics) – targets meshwork, ablating, I&A, electrocautery
- iTrack250A Microcatheter (Ellex) – enlarge schlemm's canal then tear it open by removing catheter

Trabectome (NeoMedix)

- One use disposable device
- Bipolar electro-surgical pulse 550KHz/0.1w incr
- Similtaneous irrigation & aspiration
- Ablation of TM and unroofing of schlemm's canal and juxtacanalicular tissue
- Average IOP decreases from 24mm to 15mm @60m
- Topical Rxs decrease from 3 to 1 @60m
- Advantage – easy, outpatient, option to delay trabeculectomy, less side effects

JAM

Glaukos iStent Trabecular Bypass

- Smallest medical device approved by FDA
  - 1mm long, 0.33mm height, snorkle 0.25mm x 120um, 60ug
  - Nonferromagnetic titanium single use, sterile inserter
- Approved for mild-moderate glaucoma
- Placed during cataract surgery
- Spares tissues damaged by traditional procedures
- Contraindicated in NVG, PAS, primary or secondary angle closure glaucoma, angle abnormalities
- Adverse events – corneal edema, loss of BVA>1 line, PCO, stent obstruction

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 Rxs @24m
  - Alone results – 18.6mm / 0.5 Rxs @24m
    - 70% less use of medications

CyPass Micro-Stent / Transcend Medical

- Stent the supraciliary space and augments uveoscleral outflow (like iStent Supra)
- Targets suprachoroidal outflow in redirecting aqueous outflow
- Fenestraed micro-stent 6.35mm long and 510u in diameter
- Polyimide material
- Ab interno insertion is easier than other stents
- Results – reduction in IOP by 33% and 50% decrease number of medications at one year

XEN Gel Stent - AqueSys

- Gel stent is preloaded in a disposable injector with a 27-gauge needle and delivered into the non-dissected Tenon space creating a connection from the anterior chamber to the subconjunctival space
  - Bypasses Schlemm's canal entirely
- Experimental in US; Europe for mild-moderate glaucoma, & advanced w efficacy similar to trab
- Ab interno collagen pre-loaded implant of cross linked porcine gel that hydrates on insertion
  - 3 lumen sizes: 140u, 63u, 45u
  - 1mm in AC / 3mm in sclera / 2mm in subconj space
- 40% reduction in IOP at 36 months, 74% reduction in Rx
- Adverse events – hyphema, choroidal effusion

360 Degree Trabeculotomy

- One use disposable device
- Alone or combined with cataract surgery
- Canaloplasty = 44% IOP reduction
- Tears and unroofing of schlemm's canal and juxtacanalicular tissue
- Average IOP decreases from 24.4mm to 13.7mm
- Topical Rxs decrease from 1.5 to 0.2 @12m
- Advantage – easy, outpatient, option to delay trabeculectomy, less side effects

JAM

360 Degree Trabeculotomy

- iTrack catheter 250u
- Initial use was for childhood glaucoma with poor prognosis, Failed goniotomy, infantile glaucoma after cataract surgery, infantile glaucoma associated with ocular or systemic conditions, progressive congenital glaucoma and corneal clouding
- Outcomes 87-92% successful
- Trabeculotomy codes already exist
- Formerly iScience Surgical
- Now iScience Interventional, Menlo Park CA

JAM

ExPress Mini-Glaucoma Implant (Optonol Ltd)

- Less time consuming than larger tubes
  - Allows for more extensive surgery later if needed
- Placed under scleral flap
- Conjunctival dependent
- Creates posterior low diffuse bleb within 1-2 days
- Device is 400um wide x 3mm long stainless steel device
- Avoids trabeculectomy failure

Trabeculectomy Filtering Surgery

- Conjunctival flap fornix-based
- Half thickness scleral dissection of flap
- Full thickness fistula into anterior chamber and removal of TM
- Replace scleral flap
- Loosely suture corners of flap
  - Can be cut with blades or laser later to release more fluid
  - Used to avoid post-op flat chambers and reformations
- Inject anti-metabolite
- Close conjunctiva

JAM

Trabeculectomy Complications

- Over filtration and post op flat chambers
  - Need for reformations
- Infection of bleb
- Cataract formation
- Filter failure with young, fast healers or ocular inflammatory diseases
- Alteration of tear film
- Droopy lids or visible expanding blebs
- Conjunctival dependent
- Long term failure/repeat surgery

JAM

Trabeculectomy Complications

- Shallow or flat chambers
- Choroidal detachments
- Hypotony maculopathy
- Hyphema
- Bleb leak
- Bleb infection
- Inadequate fistula and bleb failure
- cataracts

Glaucoma Tube Implants

- Developed for patients with high risk of failure from standard surgery
- Design – silicone rubber tubing and ridged plastic or silicone rubber explant
  - Materials do not allow fibroblast to adhere to device
  - Equatorial placement of explant
    - Anterior edge of explant is 8-10mm posterior to corneoscleral junction
  - Tube into anterior chamber by 2mm
  - Superior temporal position is preferred
  - Patching material required to adequately cover implant
    - Sclera, dura, pericardium

Glaucoma Tube Implants

- Drain – allows flow of aqueous from anterior chamber through tube into implant
  - Passive diffusion into surrounding peri-ocular tissues
  - Uptake by lymphatic system and venous capillaries
- Available Implants
  - Non-valved
    - Molteno
    - Baerveldt
  - Valved
    - Ahmed
    - Krupin
  - Single plate and double plate designs

Glaucoma Tube Implants

- Indications
  - Failure of conventional therapies
    - Topical
    - Laser
    - Trabeculectomy with or without MMC
  - Conjunctival diseases, pemphigoid, chemical injuries, severe dry eyes, trauma related glaucoma with scleral thinning, uveitic glaucoma, congenital glaucoma,
  - Neovascular diseases – Neovascular glaucoma, diabetic retinopathy, retinal vascular occlusions.

Glaucoma Tube Implants

- Special intra-operative and post-operative considerations
  - Temporary ligature of drain tube of non-valved implants
    - 2-4 weeks
    - Allows capsule to develop
    - Resistence to flow is established
    - Best completed with absorbable external suture or prolene suture placed into tube
      - Removed via small conjunctival incision in office
- Complications
  - Corneal endothelial issues in vicinity of tube, hypotony, obstruction of tube with fibrin, vitreous, blood, epithelial ingrowth

Baerveldt Implants (Abbott Medical Optics)

- 3 models
- Larger surface area plate than single quadrant devices
  - Single quad insertion
  - Decreased bleb height
- Smooth polished pliable silicone plate
- 4 fenestrations to promote fibrous adhesions
  - Reduces bleb height
  - Open drainage tube
  - Fixation sutures holes

Human Allograft Tissue

- Biocompatible for leaking blebs or exposed implants
- Gamma sterilized
- 2.5 year shelf life
- Nominal thickness 0.5mm
- Freeze dried or hydrated
- Available as sclera, pericardium

JAM

New Use for "Rejected" Corneas

- Journal of Glaucoma, Girkin UAB
- Donor corneas not suitable for cornea transplants (clarity) may be a better option to cover glaucoma shunts than traditional pericardium tissue
  - More durable, less likely to erode
  - Safer, lower risk of infection
  - Reduces subsequent surgery

Ahmed Implant (New World Medical Inc)

- One way valve design
  - Prevents post op hypotony
- Immediate IOP reduction
- Single stage procedure
- Eliminates "rip chord" sutures, occluding sutures, or tube ligature sutures

New Ahmed Glaucoma Valve – M4

- Valved with venture flow technology
- Thinner profile
- **Biocompatible porous polyethylene**
- **Allows soft tissue growth into pores**
- **Promotes integration and vascularization of implant**

Molteno Impants (Molteno Ophthal Ltd

- Single or double plates devices
- Double plate devices allow for greater aqueous drainage
- Silicone
- Low profile
- Larger, thinner devices

Cataract Surgery in Glaucoma Patients

- Combined surgery indications
  - Glaucoma treatment failing with topicals
  - Significant disc changes and visual field damage
  - Transient elevations of IOP associated with surgery or topical steroids may cause further damage
  - Cataract surgeons should spare conjunctiva superiorly for future placement of filters or implants
  - Benefit of definitive surgical solution to both problems with one operation

Glaucoma & the Brain

- Researchers view Glaucoma as a disease of the brain
  - Neurodegenerative disease
- Glaucoma shares common features with AD, Parkinson's and Lou Gehrig's diseases
- Offers potential for new treatments that promote nerve health, neurotrophic factors which can help at multiple places in the visual pathway
  - Neuroprotection – Ciliary neurotrophic factor (CNTF)
  - Neuroregeneration – increase axon regrowth
  - Neuroenhancement – improve support between dying RGC and surrounding cells in brain and retina

Neuroprotectants

- Memantine (Nameda) –blocks Na, K channels, retards apoptosis
- Brimonidine(?)
- Ciliary neurotrophic factor – CNTF phase I as implant
- BDNF – inhibits programmed cell death
- Erythropoetin- EPO
- Future is neuroprotection to improve environment and
  - neurodegeneration with stem cells
  - Neuroenhancement supports injured RGCs before they die
  - Immunobiology with T cell based vaccination

Neuroprotection in Glaucoma

- Tsai Curr Eye Res 2005
- EPO (erythropoetin) found to have protective effect on RGCs
  - Currently approved and well understood for anemias, post chemo-therapy, and renal diseases
- Others under study include brimonidine, memantine, BDNF
- Future will be neuroprotection to improve environment and neuroregeneration with stem cells

Nanosensor IOL

- Fraunhofer Institute in Germany
  - Microelectric Circuits and Systems IMS
- Implant sensor for continuous IOP monitoring
- Integrated a 2.5 by 2.6 millimeter sensor in an IOL
- The top and bottom of the sensor are electrodes
  - The top electrode is flexible, bottom of the sensor is rigid
  - When the intraocular pressure increases, the top electrode is pushed in, reducing the distance between the top and bottom of the sensor and thus increasing the capacitance
- Implant sends the pressure data to a reader that is fitted into the frame of a pair of spectacles
- An antenna in the spectacle frame supplies the sensor with the required energy via an electromagnetic field
- Currently undergoing clinical trials
- Could come available in two to three years time

Nanosensors IOP

- MIT Technology Review
- A pressure sensor to measure glaucoma IOP
- Tiny microchip implanted subretinal
- The sensor is designed to measure IOP
  - wirelessly transmit the data to computer
- One of the major obstacles in creating this type of device is designing a tiny but highly functional chip that uses very little power
  - Sensor runs on nanowatts rather than on microwatts
- The researchers began testing the implant in animals last December

Thank you

McGreal Educational Institute

Missouri Eye Associates

Excellence in Optometric Education

The Latest Trends in Contemporary Medicine

John A. McGreal Jr., O.D.
McGreal Educational Institute

2016

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JAM

Neurologic / Psychiatric

- Schizophrenia
  - Atypical Antipsychotics
    - Quetiapine (Seroquel)
    - Olanzapine (Zyprexa)
    - Effects reduce dopamine, increase risks of diabetes and stroke

JAM

Psychiatric

- Depression – unipolar depression refers to depression in patient's who never have experienced a manic episode. It occurs more often in females and has strong familial and genetic predispositions. Some depressions are in response to stressful situations (reactive) and others (endogenous) result from disturbances in brain chemistry. Modern hypotheses of depression postulate dysfunction in noradrenergic and serotoninergic pathways or receptor sites
- Affects 18 million Americans
- $12.6 billion drug market

JAM

Psychiatric

- Depression – prominent or persistent depressed or dysphoric mood, nearly every day for at least 2 weeks, interferes with daily activities, and 5 of these 9 symptoms are present
- Symptoms – depressed mood, loss of interest in usual activities, change in weight or appetite, insomnia or hypersomnia, psychomotor agitation or retardation, increased fatigue, feelings of guilt or worthlessness, impaired concentration, suicidal attempt or ideation

JAM

Psychiatric

- Depression – antidepressant treatments consist of tricyclics and selective serotonin reuptake inhibitors which inhibit the reuptake of norepinephrine and/or serotonin at the nerve terminals. Monoamine oxidase inhibitors (MAOIs) prevent the breakdown of norepinephrine and serotonin and prolong their effects at the nerve terminals. Electroconvulsive therapy is effective therapy in severe, medication-refractory life threatening (acutely suicidal) depression. 80% relapse on D/C
- Cognitive-Behavior Therapy - Intensive single and group counseling with psychology and social workers is necessary to address unresolved issues from past experiences which may be causative. 25% relapse on D/C

JAM

Psychiatric

- Depression / SSRIs
  - Citalopram (Celexa)
  - Escitalopram (Lexapro)
  - (Cymbalta)
  - Paroxitine (Paxil CR)
    - Depression, PD, SAD, OCD, GAD and now for PMDD
  - Fluoxetine (Prozac*Weekly*)
  - Sertralazine (Zoloft)
    - Depression, OCD, PD, PTSD
    - Children Studies – Zoloft works best, Prozac becoming new gold standard, Paxil not recommended for <18yrs
- Depression / Tricyclic antidepressants
  - Protriptyline (Vivactil), Doxepin (Sinequan)

JAM

Vortioxetine

- Indicated – Major depressive disorder MDD in adults
- Dose – 10mg qd (5/10/15/20mg)
- Contraindicated – in MAOI patients
- SE – sweeling in & around eyes, eye pain, low Na, serotonin syndrome, increased bleeding or bruising, manic episode
- Available as - ***Brintellix***

Vilazodone

- Indicated – Major depressive disorder
- Contraindicated – in MAOI patients, watch for suicidation
- Available as - ***Viibryd***

Infant Mental Health

- Birth to age 3 - “couch to crib”
- Developmental diagnostic manual updated
  - Two new subsets of depression
  - Five new subsets of anxiety
  - Six new subsets of feeding behavior disorders
- References
  - Zero to Three / Zerotothree.org
  - Interdisciplinary Council on Developemental and Learning Disorders / icdl.com
  - Floortime.org

JAM

Psychiatric

- Depression / Miscellaneous
  - Venlafaxine (Effexor)
  - Mertazapine (Remeron)
  - Nefazodone (Serzone)
  - Protriptyline (Vivactil)
  - Bupropion (Wellbutrin, SR, XL)
  - Thioridazine
- Depression / Monoamine Oxidase Inhibitors (MAOIs)
  - Phenelzine (Nardil)
  - Tranylcypromine (Parnate)

JAM

New Approaches to Depression

- CRF1 antagonists – reduces cortisol
- Mifrpristone – reduces cortisol
- V1B antagonist – reduces cortisol
- Agomelatine – regulates sleep-wake cycle
- Metabotropic glutamate receptor 5 antagonist – slows excitability
- Nicotine – controls mood fluxuation
- NK1,2 – pain receptors

JAM

Tobacco Use

- Single greatest health hazard existing in USA. 400,000 deaths per year related to cigarette use, mostly cancer of the lung or cardiovascular mortality.
- Estimated that an individual who smokes 1 PPD starting at age 15 loses approximately 7 minutes of life per cigarette inhaled.
- Also increased risk of cancer of the tongue, esophagus, stomach, colon, cervix, bladder. Increased risk of chronic bronchitis and emphysema.
- Passive smoking (second hand) has many risks (cancer, COPD, asthma) as well. Nicotine is addicting both physiologically and psychologically and recidivism after initially quitting is quite high

JAM

Lung Cancer

- Malignancies may be primary (75%) or metastatic (25%) cancer. Characterized by histologic characteristics of the tumor. Major types are
  - squamous cell carcinoma
  - Adenocarcinoma
  - large cell carcinoma
  - small cell carcinoma.
- Nearly 150,000 deaths per year in USA from cancer, most common cause of cancer death in men and just passed breast cancer in women . Single most important cause of cancer is cigarette smoking. Other causes include radon, radiation, vinyl chloride, hydrocarbons, asbestos
- Symptoms are localized and include dyspnea, cough, hemoptysis, chest pain, pneumonia, Horner's syndrome

JAM

Lung Cancer

- Most caused by cigarette smoke (90%)
- 25% of adult women smoke
- 30% of high school women smoke
- 13-22% of pregnant women smoke
- Cessation of smoking
  - Quit by 35 = 6-8 years of life expectancy
  - Quit by 44 = 6-7 years of life expectancy
  - Quit by 55 = 3-6 years of life expectancy
  - Quit by 65 = 1-4 years of life expectancy
  - 55% decrease in heart attack after quitting for one year!

JAM

Tobacco Use

- 10% of people over age 65 smoke
- 14.2 billion spent last year in Medicare to address smoking related illness
  - 10% of the entire Medicare budget
- New Medicare counseling program offered to beneficiaries to help with cessation programs
- Leading cause of preventable morbidity & mortality in US
- Cigarette smoking is significantly associated w new onset uveitis (Ophthal, 2015 122: 1257 Yuen,B et al)

JAM

Smoking Cessation

- 1-7% chance of quitting without help
- Antidepressants
  - Bupropion (Wellbutrin/Zyban)
- Nicotine replacement
  - Nicodern CQ Patch (Transdermal Nicotine 21mg, 14mg, 7mg steps over 10 weeks)
  - Nicorette Gum (2mg if <25 cigarettes/D, 4mg if >25 cigarettes/D)
  - Nicotrol Inhaler
  - Nicotrol Nasal Spray
  - Nicotrol Patch

JAM

Smoking Cessation

- Best new option
  - Varenicline (Chantix/Pfizer)
    - 43.9% quit vs 29.8% quit on bupropion
    - Treatment is for 12 weeks, if successful take it 12 more weeks to lessen chance of smoking again
    - Blocks nicotine receptors in brain and stops "reward" associated with smoking again
    - Side effects – nausea is mild and tolerable but occurs at 32%, 3% discontinued

JAM

Roflumilast

- Indicated – treatment to reduce risk of COPD exacerbations in severe COPD associated with chronic bronchitis and history of exacerbations
- Side effects – psychiatric, usually suicide thoughts or depression
- Available as - ***Daliresp***

Umeclidinium & Vilanterol

- Indicated – treatment of COPD and chronic bronchitis and emphysema in adults
  - Not approved for asthma
- One inhalation per day
- Side effects – sore throat, watch blood glucose and potassium
- Available as – ***ANORO***

Psychiatric

- Anxiety Disorders – adaptive psychophysiologic reaction to acutely stressful situations. Pathologic anxiety can be generalized (GAD), can occur in discrete panic attacks or can be associated with avoidant (phobic) behavior. GAD unrealistic , excessive anxiety & worry about 2 or more life circumstances for 6 months or more, at least 6 of the following symptoms are present

JAM

Psychiatric

- Anxiety Disorders
  - Symptoms / Motor tension – trembles, twitches, soreness, restlessness
  - Symptoms / Autonomic hyperactivity – Shortness of breath, palpitations, cold & clammy, nausea, vomiting, irritable, lump in throat
  - Symptoms / Vigilance and scanning – keyed up, on edge, decreased concentration, trouble falling asleep or staying asleep

JAM

Psychiatric

- Anxiety / Benzodiazepines
  - Lorazepam (Ativan)
  - Chlordiazepoxide (Librium)
  - Clorazepate (Tranxene)
  - Diazepam (Valium)
  - Alprazolam (Xanax)
    - GAD
- Anxiety / Miscellaneous
  - Paroxetine (Paxil)
  - Venlafaxine (Effexor, XR)
  - Doxepin (Sinequan)

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Psychiatric

- Insomnia – non diazepines
  - Zolpidem (AmbienCR)
  - Eszopiclone (Lunesta)
  - Zaleplan – (Sonata)
  - Ramelteon (Rozerem)
- Suvorexant (Belsomra) - first in class to target orexin neurons in brain arousal circuits (wakefulness center)
  - Speeds onset and reduces nighttime awakenings
  - 4 doses
- Restless Leg Syndrome
  - Ropinirol (Requip)

JAM

Neurologic / Psychiatric

- Headache
  - Sumatriptan (Imitrex NS, tablets, SQ stat)
  - Zolmatriptan (Zomig)
  - Naratriptan (Amerge)
  - Rizatriptan (Maxalt)
  - Eletriptan (Relpax)
- Migraine recognized as an organic disease
  - Brain lesions visable

JAM

Neurologic / Psychiatric

- Attention Deficit Hyperactivity Disorder (ADHD) – disorder of children and adults characterized by inability to concentrate, short attention span, hyperactivity, emotional liability, impulsivity, distractibility
- 1/3rd ADHD in children linked to tobacco smoke before birth or lead exposure afterward (environment)
- Treatment
  - Methylphenidate (Ritalin)
  - Clonidine (Catapres)
  - Dextroamphetamine (Adderall XR)
  - Atomoxetine (Strattera)
  - Methylphenadate (Concerta)
  - "black box" warnings for amphetamines recommended by FDA

JAM

Neurologic

- Multiple Sclerosis
  - Glatiramer (Copaxone)
  - Interferon B-1b (Betaseron)
  - Interferon B-1a (Avonex)
  - Interferon B (Rufab)
    - Side effects – macular edema, CRVO, CRAO, CWS, optic neuritis, papilledema
    - Flu-like symptoms are common for 2 weeks
    - Medications are given by injection
    - Annual costs range from $12,000-$33,000/year

JAM

Dimethyl fumarate

- Indicated – treatment of relapsing multiple sclerosis
- Oral
- SE – rare brain infection, white blood cell count decreases, flushing, stomach upset
- Available as - ***Tecfidera***

Gastroenterology

- Irritable Bowel Syndrome with Diarrhea
  - Lessens bowel contraction
  - Reduces abdominal pain
  - Improves stool consistency
- Eluxadoline – Viberzi

JAM

Hepatitis-C Breakthrough

- Chronic hepatitis C virus genotype 1
- CURE rate 94-99%
- Interferon ribavirin free tablet
- Once daily
  - 8 weeks in treatment naive patients
  - 24 weeks in treatment experience patients
  - Side effects – fatigue, HA
  - High cure rates achieved even in cirrhosis, previous treatment, advanced age and high BMI
- Ledipasvir / Sofosbuvir – Harvoni

JAM

Neurologic

- Optic Neuritis
  - Controlled High-Risk Avonex Multiple Sclerosis Study (CHAMPS), Optic Neuritis Treatment Trial (ONTT)
    - Initial demylinating episode (like ON) treated with interferon
      - Conclusively showed that treatment with interferon slowed rate of development of MS
    - Do not use oral steroids to treat ON
    - *Brain MRI obtained in all patients with ON*
    - If MRI abnormal IV/oral steroid regimen should be used
      - IV methylprednisolone 100mg q6h x 3d, followed by PO prednisone x 11 days
    - Abnormal MRI should be referred to neurologists for consideration of interferon treatment

Neurologic

- Optic Neuritis
  - Optic Neuritis Treatment Trial (ONTT)
  - Archives Ophthalmology 2003
  - Reported 10 year risk of developing MS is significantly higher if there is a *single brain lesion noted on MRI* scan at the time diagnosis (56% vs. 22%)
  - The overall 10 year risk is 38%
  - Male gender, no lesions on MRI and presence of disc swelling places a patient at lower risk of developing MS

Neurologic

- Internuclear Ophthalmoplegia (INO)
  - Lesion of the medial longitudinal fascicules (MLF) in pons
  - Adduction deficit and contralateral abduction nystagmus
    - Named for side of adduction deficit
    - Seen in MS, stokes, metastatic lesions
    - Bilateral lesions are very suggestive of MS (BINO)

Neurologic

- Parkinsonism
  - Degenerative disease characterized by resting tremor, rigidity and bradykinesia results from loss of dopaminergic neurons in substantia nigra of the midbrain in patients over age 50, accompanied by depression in many. Progresses to include dysmetria and intention tremor.
  - Treatment
    - L-dopa
    - Pramipexole (Mirapex)
    - Ropinirole (Requip)
      - FDA approved as first and only treatment for Restless Leg Syndrome

Neurologic

- Seizure Disorders (Epilepsy)
  - Distinct episode of excessive, uncontrolled electrical activity (ictus) occurring in the brain characterized by indiscriminate firing of neurons. Seizures are brief and followed by the post-ictal period of decreased cerebral activity with lethargy, confusion and focal neurologic dysfunction. Seizures may be primary or secondary to injuries, infections
  - **Grand mal epilepsy**
    - idiopathic, loss of consciousness and bowel/bladder control, tonic (contraction)/clonic (jerky) phases
  - **Petite mal epilepsy**
    - disorder of childhood, momentary loss of consciousness, little loss of control, stops in adolescence in many.
  - **Jacksonian seizure**
    - begins with jerky muscle movement in an isolated limb which spreads to adjacent muscle groups

Neurologic

- Seizure Disorders (Epilepsy) – Treatment
  - Topiramate (Topamax)
    - Also useful im migraine management
    - Small risk of angle closure
  - Tiagabine (Gabitril)
  - Gabapentin (Neurontin)
    - Also useful in post herpetic neuralgia
    - Up to 1800mg/Day
  - Pregabalin (Lyrica)
    - Post-herpetic neuralgia
    - Diabetic peripheral neuropathy
    - Partial onset seizures in adults

Gabapentin (Horizant)

- Anti-seizure drug Neurontin
- 1st non-dopaminergic treatment
- Indicated – moderate to severe primary restless leg syndrome

Neurologic / Psychiatric

- Alzheimer's Dementia – chronic, progressive deterioration in global intellectual functioning. Familial tendencies, associated with B- amyloid and organic changes in the brain. 4.5 million Americans diagnosed
  - Research at Boston University
    - 2,581 patients
    - 79% reduction in risk of developing AD
    - Statins reduce cholesterol by blocking enzyme HMG Co-A reductase
    - Also interfere with production of B-amyloid
  - Current treatments target anticholinesterase, target amyloid production and gamma secretase

JAM

Neurologic / Psychiatric

- Alzheimer's Dementia
  - Donepezil (Aricept)
  - Tacrine (Cognex)
  - Rivastigmine (Exelon)
  - Galantamine (Reminyl)
- Experimental drugs with promise include Gleevec/Novartis which targets proteins that regulate secretase, sage extract, raloxifene, huperzin A (cholinesterase inhibitor, Chinese herb)
- Combinations with Memantine (Namenda) are safe and effective in moderate to severe AD
- Regular exercise in midlife reduce risk of AD by 50% (Lancet Neurol 2005)
  - 20-30 minutes of exercise twice a week

JAM

Memantine & Donepezil

- Indicated – treatment of moderate to severe AD
- Combination of two previously used individual drugs
- Dose – 14/10 or 28/10
- Once per day
- Side effects – slow heart beat, nausea and vomiting, HA most common, diarrhea, dizziness
- Available as – ***Namzaric (Activis)***

Neurologic / Psychiatric

- Alzheimer's Dementia – 50% develop psychiatric and behavioral symptoms
  - Anxiety, aggression/violent outbursts, paranoid thoughts
  - Treatment trials and "off-label" use of Depakote
    - Inhibits tangles and plaques
    - May prevent psychiatric symptoms
  - Rule out UTI, thirst, hunger, pain, medication side effects

JAM

Neurologic / Psychiatric

- Acute Ischemic Stroke
  - 700,000/yr or one every 45 seconds
    - 500,000 new, 200,000 recurrent
  - 164,000 deaths/yr, 3rd leading cause of deatths
  - Cost $56.8 billion in 2005
- Risk factors – HTN, smoking, DM, artery diseases, African-Americans twice prevalence
- Treatment
  - Alteplase (Activase)
  - Carotid artery stents – option in CA endarterctomy
  - Brain stents – Boston Scientific's Wingspan

JAM

Antaging

- Calorie restriction (CR) – cutting normal calorie intake by 1/3rd boosts animal lifespans by 30-40%
- Resveratrol – proven at Harvard & National Institute on Aging to extend lifespan by 20%, slow aging process, even with high calorie diet
  - Studies in fruit flies, mice, fish, now humans
  - Present in red wine

JAM

Deoxycholic acid

- Indicated – treatment of submental fat
- Dose form - injection
- SE – injection sitr redness
- Available as - ***Kybella***

Tavaborole 5%

- Indicated – toenail fungus
- Topical solution
- Not for children or pregnancy
- SE – redness at application site
- Available as - ***Kerydin***

New Alcohol

- March 2015 Alcohol Tax & Trade Bureau approved powdered alcohol products (Palchol) for sale in US
  - Absorbed into carbohydrate dextrin resulting in dry state
  - 50% by weight, if mixed according to package would yield 10% alcohol by volume
- Problems – higher dose mixes, binge drinking, undermining retail business, undermining taxation and regulation, spiking non alcohol beverages, easy consealment at facilities not permitting alcohol, promote smuggling over state lines, undermining retail responsibility laws, social issues & fatalities (100,000)

JAM

Antibiotic vs Appendectomy ?

- Assumed progression of appendicitis from mild disease to perforation with appendectomy as only means of preventing serious infection became established thought
- Several trials suggest that treating CT-confirmed uncomplicated appendicitis with initial round of antibiotic Ertapenem is successful in 73% over a one year period. Of those who did require surgery for failure to improve or presenting with recurrent appendicitis, there was no complication from receiving antibiotics
- JAMA 2015;313(23) Salminen, et al

JAM

Cardiovascular

- New Guidelines for Blood Cholesterol Treatment
  - Heart disease is the number 1 killer in this country
  - 65 million Americans should change life-style & diet (50)
  - 36 million should take medications to lower cholesterol (13)
  - Many more patients are now candidates for drug treatment than previous
  - many recent studies confirm a dramatic decrease in mortality and morbidity associated with decreased cholesterol levels
  - Framingham Heart Study “risk calculator”

JAM

Cardiovascular

- National Cholesterol Education Program Adult Treatment Panel (NCEP ATP-III) – lipid management in USA is less than desirable
  - <50% of even highest risk patients receive lipid lowering treatment
  - 1/3rd of treated patients achieve LDL goal
  - <20% of CHD patients achieve LDL goal
  - <50% of patients who are prescribed lipid lowering drugs are still taking it six months later, 30-40% after 12 months
  - 1 in 8 MI patients quit drugs only 1 month after discharge and are 3 times more likely to die in the year after MI

JAM

New Cardiovascular Concepts

- >20 years old = lipoprotein profile
  - LDL, HDL, Triglycerides, total cholesterol, and BP
- Guidelines
  - Total cholesterol <200 <200 (175)
  - LDL <130 <130
  - LDL (high risk) <130 <100 (70)
  - HDL >35 >40
- Risk Factors
  - Gender, age, smoking, high total cholesterol or LDL, low HDL, HTN, family history premature heart disease, & obesity

JAM

New Cardiovascular Concepts

- Risk Factors
  - Diabetes now singled out as so potent risk factor and assumes high risk category (same as for previous MI)
  - "metabolic syndrome" - new risk factor
    - requires three or more of the following
      - abdominal obesity - 40 in men/35in women
      - low HDL -<40 men/<50 women
      - fasting triglycerides >150
      - HTN
      - fasting glucose >110
- New Concepts – C reactive protein, apolipoproteins, adiponectin protein, treat HDL & LDL together

JAM

Cholesterol Guidelines

- More than half of the coronary artery disease in the U.S. is attributable to abnormalities in the levels and metabolism of plasma lipids and lipoproteins. Diabetes, alcohol consumption, OCs, renal disease, hepatitic disease, hypothyroidism can worsen hypercholesterolemia or worsen underlying hyperlipoproteinemia.
- LDL = total cholesterol – HDL – triglycerides / 5.
- Every 1% reduction in TC yields a 2% reduction in CAD risk!

JAM

Cholesterol Guidelines (ACC/AHA) 2013

- Pts with ASCVD inc MI, angina, previous coronary revascularization
- Pts w/o clinical ASCVD but w LDL-C >190mg/dl
- Pts 40-75 yrs w/o clinical ASCVD but w DM and LDL-C from 70-189mg/dl
- Pts 40-75 yrs w/o clinical ASCVD and DM but w LDL-C from 70-189 and estimated 10 year ASCVD risk of 7.5% or higher
- For the first three groups there is universal acceptance of data
- The fourth group triggered immediate controversy
- JAMA 2015;(2):142-150 Pandya et al Cost Effectiveness of 10 yr Risk Thresholds of Statin Therapy for Primary Prevention of CVD

JAM

Cholesterol Guidelines (ACC/AHA) 2015

- Two new reports in JAMA 2015 suggest that the new risk factor threshold is reasonable and cost effective
- Suggest it may not even go far enough
- Included a more lenient and cost effective threshold taking into consideration patient preferences for daily pill, changes to statin prices, and risk of statin induced diabetes
- Could lead to massive treatment of billions of people worldwide
- We finally know who and when to treat with a cost effective primary prevention strategy

JAM

US Dietary Guidelines 2015

- USDA and HHS jointly release new guidelines every 5 years
- Far reaching influences on food supply across government cafeterias, schools, military, food assistance programs, agricultural products, restaurant recipes, industry food formulations; Revisions of guidelines is necessary for the health of millions
- Eliminates cholesterol as a nutrient of concern
  - No appreciable relationship between dietary cholesterol and serum cholesterol
- Absence of upper limit on total fat consumption
  - Dieatry advice should emphasize optimizing types of fat not reducing total fat, since so often low fat is replaced w carbs

JAM

US Dietary Guidelines 2015

- Other policies need to follow suit but nothing is consistent
- Nutrition Fact Panel – separately regulated by FDA uses 30% fat limit obsolete for over a decade
- US Dept of Agriculture – should modernize the Smart Snacks in School standards removing 35% restriction on total fat
- Institute of Medicine – should update its report on dietary reference intakes for energy and macronutrients, now over 15 years old
- National Institute of Health guidelines recommends caution eating nuts, tuna canned in oil, olive oil, vegetables cooked w added fat, same category as chips, soda, and candy
- Natioanl School Lunch Program – bans whole milk, allows sugar sweetened non-fat milk

JAM

Lipids

- Cholesterol
  - Normal <200mg/dl
  - Cholesterol is used by the body to form steroid hormones, bile acids, and cell membranes.
  - Increased – cardiovascular disease and ateriosclerosis, jaundice, uncontrolled diabetes
  - Decreased – malabsorption syndromes, stress, sepsis, liver disease, hyperthyroidism
  - Interfering factors – pregnancy, many drugs
- Framingham Heart Studies – 1/3rd of all MI patients have cholesterol <200. The implication is that "normal" levels are probably not normal at all

JAM

Lipids

- Low Density Lipoproteins (LDL)
  - Normal: 130mg/dl, High risk: 100mg/dl (70mg/dl since 7/04)
  - LDL is the cholesterol rich remnants of the lipid transport vehicle, VLDL.
  - Increased – coronary heart disease, atherosclerosis
  - Modifications – losing weight, moderate alcohol consumption, niacin supplements, exercise, less red meat, less dairy, limit saturated fat, no fried foods, may all decrease LDL

JAM

Lipids

- High Density Lipoproteins (HDL)
  - Normal: 45mg/dl
  - HDL is the cholesterol carried by alpha lipoproteins. A high HDL is an indication of a healthy metabolic system in a person free of liver disease. HDL serve as transporters of cholesterol and carry it from peripheral tissues to liver for catabolism and excretion. HDL probably inhibit uptake of LDLs.
  - Increased – chronic liver disorders
  - Decreased – in coronary artery disease, chronic physical inactivity, long distance runners, Lumigan??
  - Modifications – losing weight, moderate alcohol consumption, lecithin supplements, exercise, less red meat may all increase HDL, torcetrapib not approved!

Lipids

- Triglycerides
  - Normal: 0-150/dl, lower in females, higher with age
  - Triglycerides are produced in the liver from glycerol and fatty acids. They are used for production of energy. Excess levels of triglycerides are stored in adipose tissue.
  - Increased – atherosclerosis, liver disease, pancreatitis, MI, hyperlipoprotinemias, toxemias, nephrotic syndromes
  - Decreased – malnutrition, congenital lipoproteinemias
  - Modifications – losing weight, low fat diet, exercise

Cholesterol Guidelines

- Disorders of Lipid metabolism
  - **Isolated Hypercholesterolemia** – TC>200, TG normal
    - Familial Hypercholesterolemia (FH) – genetic disorder, TC 275-500, TG normal, HDL normal or reduced
    - Familial Defective APO B – autosomal dominant, phenocopy of FH
    - Polygenic Hypercholeserolemia – mixed form, multiple genetic defects and environmental factors like age, sex, diet, exercise. TC<350
  - **Isolated Hypertriglyceridemia** – TG>200 (chylomicrons or VLDL are increased)
    - Familial Hypertriglyceridemia
  - **Hypercholesterolemia and hypertriglyceridemia**
    - Familial Combined hyperlipidemia (FCHL)

JAM

Cholesterol Lowering Drugs

- Lipid Lowering – HMG Co-A reductase inhibitors
  - Atorvastatin (Lipitor) – 9.2B
  - Lovastatin (Mevacor)
  - Pravastatin (Pravacol) – 2.8B
  - Simvastatin (Zocor) – 5.0B, 80mg dose risky
  - Fluvastatin (Lescol) – 0.73B
  - Rosuvastatin (Crestor) – 0.13B
  - Ezetimibe (Zetia) – alone or in combination (-23% reduction in LDL-C)
  - Ezetimibel (Vytorin) – combination of Zocor & Zetia
  - Desired effects – lower LDL, reduces inflammation in coronary arteries
  - Side effects - hepatitic dysfunction (2%), myositis (1%), inc CPK
- HDL raising – torcetrapib not approved! Systolic BP 4mm higher

JAM

Pitavastatin

- Indicated – treatment of cholesterol problems
  - Reduce TC
  - Reduce LDL-C
  - Reduce ApoB
  - Reduce TG
  - Increase HDL-C
- SE – low back pain, constipation, diarrhea
- Available as - ***Livalo***

Evolocumab

- Indicated – treatment of hypercholesterolemia in statin patients who are on maximal dose but need more lowering of LDL-C
- PCSK9 inhibitor
- Dose – 140mg/ml
- self injection under skin with single use autoinjector every 2 weeks or if monthly dose is preferred then 3 injections in a row within 30 minutes
- SE – sore throat, runny nose
- Available as - ***Repatha***

Alirocumab

- Indicated – treatment of familial hypercholesterolemia in statin patients who are on maximal dose but need more lowering of LDL-C and in pts w heart attack or stroke
- PCSK9 inhibitor Dose – 75mg/ml
- self injection under skin with single use autoinjector every 2 weeks or if monthly dose is preferred then 3 injections in a row within 30 minutes
- SE – sore throat, runny nose
- Costly - $560/injection or $14,500 per year
- Available as - ***Praluent***

Cardiovascular

- Lipid Lowering Margarines
  - Benecol (McNeil)
  - TakeControl (Unilever)
  - Smart Balance (Trans-fatty acids)
- Drug eluting stents
  - Boston Scientific – Taxus stent
  - Johnson & Johnson – Cypher stent

JAM

Cholesterol (TG) Lowering Drugs

- Nicotinic acid
  - Niacin 50-100mg tid initially, then increase to 1-2.5g tid
  - Side effects: flushing (ASA helps), arrhythemias, pruritis
- Bile acid –binding resins
  - Cholestyramine (Questran)10g bid
  - Cholestipol (Cholestid) 10g bid
  - Side effects: constipation, bloating, discomfort
- Fibric acid derivatives
  - Clofibrate (Atromid)
  - Gemfibrazole (Lopid)
  - Fenofibrate (Tricor)
  - Side effects: gallstones, nausea
- No fat diet, fish oils also help lower TG

JAM

Hypertension

- Characterized by chronic elevation of BP >140/90. Etiology unknown in 90-95% (essential hypertension). Consider a secondary correctable form of HTN in pts under 30 or those who become HTN after 55. Isolated systolic HTN (systolic>160) and diastolic <90 most common in elderly due to decreased vascular compliance.
- Secondary HTN – causes include renal artery stenosis, renal disease, coarctation of the aorta, pheochrmocytoma, hyperaldosteronism (hypokalemia), other causes (thyroid disease, acromegaly, OCs, Cushing's syndrome)

JAM

Hypertension

- Laboratory tests – creatinine, BUN, UA, CXR, ECG (LV hypertrophy suggests chronicity of HTN), blood tests may include CBC, glucose, cholesterol, triglycerides, calcium, uric acid.
- Treatment – goal is control with minimal side effects on monotherapy if possible. First line agents include *beta blockers* (effective in young), *ACE inhibitors* (well tolerated with low frequency of side effects, angioedema, rash, or non-productive cough, contraindicated in pregnancy), *calcium channel antagonists* (direct arteriolar vasodilators, may cause bradycardia so avoid combination with B-blockers), *diuretics* (thiazides preferred over loop diuretics because of longer action), and *alpha adrenergic* receptor blockers.

JAM

Prehypertension

- New Guidelines for Blood Pressure Control
  - JAMA 5.21.03 National Heart, Blood, Lung Institute
  - *45 million Americans have "prehypertension"*
  - *BP = 120-139/80-90*
  - Risks are MI, kidney failure, stroke, CHF
  - Many more patients are now candidates for drug treatment than previous
  - Many recent studies confirm a dramatic decrease in mortality and morbidity associated with decreased BP levels. *Systolic blood pressure is far more important* risk factor > age 50. Damage occurs at 115/75, with each 20/10 increase doubling mortality!

JAM

Prehypertension

- New Guidelines for Blood Pressure Control
  - JAMA 5.21.03 National Heart, Blood, Lung Institute
  - *45 million Americans have "prehypertension"*
  - Damage occurs at 115/75, with each 20/10 increase doubling mortality!
  - Framingham proves 90% of those with normal BP at age 55 eventually develop HTN.
  - DASH (dietary approach to stop hypertension) diet is endorsed.
  - Start treatment with thiazide diuretic
    - Low cost, generic

JAM

Prehypertension

- The Truth About Salt
  - Institute of Medicine lowered daily sodium to 1.5g/d (3.8g/d of salt) from 2.4g/d.
  - Av individual US consumption is 4g/d! (1.5 teaspoon)
  - Americans consume 3/4ths salt from packaged food and fast food
  - Only 11% comes from salt added at the table
  - Reading labels is important as products vary in salt content
    - Campbell Soup Tomato has twice salt of Organic Valley Tomato
    - Burger King Sm Fries has three times salt of McDonalds fries

JAM

Prehypertension

- Thin crust cheese pizza (slice)
  - Little Ceasar = 210mg
  - Pizza Hut = 490mg
- French fries (small)
  - McDonalds = 140mg
  - Burger King = 410mg
- Tomato Soup
  - Health Valley organic = 380mg
  - Campbell = 760mg
- Ranch salad dressing
  - Wishbone = 250mg
  - Kraft = 280mg

JAM

Prehypertension

- Chicken sandwich
  - McChicken = 810mg
  - BurgerKing Original = 1270mg
- Cereal (30g)
  - Barbara's Honey Nut O's = 75mg
  - Honey Nut Cheerios = 190mg
- Canned Chicken Broth
  - Health Valley = 390mg
  - Swanson = 570mg
- Mild salsa
  - Chi Chi's Fiesta Thick & Chunky = 150mg
  - Pace Chunky = 230mg

JAM

Thrombolytics for MI

- Acute Coronary Syndromes
  - Reteplace (Retavase)
  - Eptifibatide (Integrilin)
  - Tirofiban (Aggrastat)
  - ASA (Bayer) 325mg chewed STAT
  - Drug-eluting stents
- Prevention
  - ASA 81mg (only 1/3rd of 62 milllion at risk in US use ASA)
    - Reduces 1st MI risk by 32%, 2nd MI risk by 20%
  - Caution in "vigorous" exercise which can contribute up to 17% of all sudden cardiac deaths

JAM

Pradaxa (dabigatran)

- Anticoagulant – 150mg
- Reduces risk of stroke in A-fib
  - 35% MORE REDUCTION IN STROKE THAN WARFARIN
  - No need for regular blood tests
  - No dietary restrictions (green leafy vegetsables)
- SE – GI 35%, heartburn, GERD, ulcers
- Cost - $7.90/day compared to generic warfarin
  - Monthly testing, co-pays, dose adjustments can be $50-$500 per month

Anticoagulants

- Anticoagulant – 4th new oral
- Direct factor Xa inhibitor
- Approved for venous thromboembolism and prevention of stroke in non-valular A-fib
- Once daily
- Cost - $277 20/mon compared to generic warfarin
  - Monthly testing, co-pays, dose adjustments can be $50-$500 per month
- Edoxaban - Savaysa

Ivabradine

- Indicated – to reduce risk of hospitalization for worsening heart failure on maximally tolerated beta blockaid
- Not for decompensated HF or low blood pressure, AV block
- Increases risk of A-Fib
- Dosed – 5mg or 7.5mg tablets
- Available as - ***Corlanor***

Belimumab / Human Genome Sciences

- Indicated – treatment of adult lupus
  - 1st new treatment in 50 years!
  - ASA in 1948
  - Plaquenil & steroids in 1955
  - Humanized IG G1y monoclonal antibody
  - Inhibits human B lymphocyte stimulator
- Dosed – IV infusion, in conjunction with standard therapies (steroids, NSAIDs, antimalarials, immune drugs)
- Available as - ***Benlysta***

Vemurafenib

- Indicated – in unresectable or metastatic melanoma
  - With the BRAF mutation
- 56% reduction in risk of death from any cause
- Requires BRAF testing result positive
- Available as - ***Zelboraf***

Genitourinary

- Prostate Disorders
  - CA is 2nd leading cause of cancer death in men after lung CA
    - UCSF & Cleveland clinic found virus infection linked to Prostate CA
  - 200,000/yr diagnosed & 30,000 deaths/yr
  - PSA gold standard is <4.0
  - New research at Washington Univ & Harvard
    - Waiting until PSA = 4 before Biopsy misses 82% CA in <60y
    - Waiting until PSA = 4 before Biopsy mises 65% of CA in >60y
    - Suggest biopsy at 2.5
    - PSA 4-10 = 25% risk of CA
    - PSA test annually >50y (earlier if positive family history, 40 to establish change rate)
    - PSA changing by more than 0.35ng/ml/yr = biopsy
    - CA risk depends on man's age, race, size of prostate, vasectomy before 35, high fate or red meat diet

JAM

Genitourinary

- Prostate Disorders
  - Tamsulosin (Flomax) -Intraoperative Floppy Iris Syndrome
  - Cancer - Vitamin E (30%) and Selinium (60%), lycopene, soy, Celebrex
- Impotence
  - Alprostadil (Caverjet) & Alprostadil (MUSE)
  - Sildenafil (Viagra) - now used before & after prostate surgery
  - Tadalafil (Cialis)
  - Vardenafil (Levitra)
- Male Birth Control Pill
  - 5 years from FDA approval, 3 months to work

JAM

Genitourinary

- Prostate Disorders
  - PSA benefits called into question
  - 2 major clinical trials both find limited benefits, but substantial harms
  - Conclusions - benefits vs risks of screening reviewed and recommend against screening in men 55-69 years old & those over age 70

JAM

Women's Health Care

- Breast Cancer
  - New approach – chemo BEFORE surgery, dose-dense chemo, hormonal drugs in post menopausal women works as well as chemo
  - Tamoxifen (Nolvadex)
  - Trastuzumab (Herceptin)
  - Letrozole (Femara) – FDA approved for use after 5 years of tamoxifen to reduce CA recurrence but will replace tamoxifen soon
  - Breastcancer.org, cancer.gov, nationalbreastcancer.org
- Premenstrual Dysphoric Disorder
  - Fluoxetine (Sarafem)
  - Paroxitine (Paxil CR)
- Unwanted Facial Hair
  - Eflornithine (Vaniqa Cream 13.9%)

JAM

Flibanserin

- Indicated – premenopausal women with generalized hypoactive sexual desire disorder
- Dose form – 100mg oral
- Non-hormonal serotonin agonist (5HT1A) and antagonist (5HT2A)
- Satisfying sexual events increase by 0.5 per month
- SE – fainting with alcohol use
- Available as - ***Addi***

Pertuzumab

- 1st line treatment of HER2 and metastatic breast cancer
- In combination with trastuzumab and docetaxel
- Only if patient has not received prior anti-HER2 therapy or chemotherapy for metastatic disease
- SE – birth defects, embryo-fetal death, diarrhea, alopecia
- Benefit – adds 18.5 months preogresion free survival
- Available as - ***Perjeta***

Women's Health Care

- Irritable bowel syndrome (IBS)
  - Tegaserod (Zelnorm)
- Psoriasis
  - Alafacept (Amevive)
- Fertility
  - Urofollitropin (Bravelle)
- Contraception
  - MirenaIUD 20ug levonorgestrel (0.1% failure)
  - ParaGardIUD (0.8% failure)

JAM

Women's Health Care

- Cervical Cancer – all linked to oncogenic HPVs
  - 3,700 deaths/yr (10 per day)
- Cervical Dysplasia
  - 330,000 new cases of high grade cervical dysplasia
  - 1.4 million new cases of low grade cervical dysplasia
- Genital Warts
  - 1 million new cases of warts in US

JAM

Women's Health Care

- Cervical cancer screening update – ACOG & ACS
  - Screening for cervical cancer starts 3 years after a woman begins to have vaginal intercourse, no later than 21
  - Annual Pap test for <30 years olds
  - Human papillomavirus (HPV) DNA testing along with Pap for women ages 30 and older
    - If BOTH are normal, than screening can be every 3 years

JAM

Sexually Transmitted Disease

- Half new cases of STDs occur in teens
  - 1 in 2 sexually active youth will contract STD by age 25
  - Half of 15-19 women HPV positive within three years of sexual initiation (Cincinnati Children's Hospital Survey)
  - Half of all new HIV-AIDS among adolescents
- Strong connection between HPV & cervical CA & warts
  - Gardasil (Merck) – vaccine near approval for ages 9-26
    - Best strategy is to vaccinate before children become sexually active
    - Vaccinate BOTH boys and girls
    - AAP (maketheconnection.org), American Social Health Association (ashastd.org)

JAM

Women's Health Care

- Lung Cancer
  - Leading cause of cancer death in US women
    - More than breast and all gynecological cancers combined
  - Most caused by cigarette smoke (90%)
  - 25% of adult women smoke
  - 30% of high school women smoke
  - 13-22% of pregnant women smoke
- Cessation of smoking (Wellbutrin/ Nicotrol Inhaler, NS / varenicline (Pfizer)
  - Quit by 35 = 6-8 yrs life expectancy
  - Quit by 44 = 6-7 yrs life expectancy
  - Quit by 55 = 3-6 yrs life expectancy
  - Quit by 65 = 1-4 yrs life expectancy
  - 55% decrease in heart attack after quitting for 1 year!

JAM

Skeletal

- Bone Disorders – Osteoporosis
  - 10 million diagnosed, 340,000 hip fractures/yr, 1yr mortality is 36%!
  - National Osteoporosis Foundation – 1 in 2 females, 1 in 4 males >50yr will have osteoporosis related fracture.
  - Peak bone mass acquired by age 18 in Females & 20 in Males
  - American Academy of Pediatrics: eliminate soft drinks in schools, swap for milk
  - Females >35y should use supplemental calcium to load bone
  - >65y supplemental calcium and vitamin D can reduce osteoporosis fracture risk by 50%

JAM

Skeletal

- Bone Disorders
  - Alendronate (Fosamax) – association with osteonecrosis of the jaw
  - Risedronate (Actonel)
  - Calcitonin NS (Miacalcin)
  - Tiludronate (Skelid)
  - Raloxifene (Evista)
  - Sodium Hyaluronate (Hyalgan, Synvisc)
  - Teriaratide (Forteo)

JAM

Skeletal

- Hormone Replacement Therapy
  - Abandon one size fits all approach
  - Consider risk factors before decision to treat with HRT
    - Risk for breast cancer / Risk for osteoporosis / Severity of symptoms
    - Short term HRT may still benefit high risk patients
    - Patches, rings, creams offer lower risks
  - Prempro study examined only one drug and one dose
    - Small increased risk with HRT
    - 8 cases of breast cancer / 10,000
    - 8 cases of stroke / 10,000
    - 7 cases of heart attack / 10,000
    - 18 blood clots / 10,000

JAM

Menopause

- Hot flashes
  - Soy foods, black cohosh, antidepressants, vitamin E, short term HRT, certain antihypertensive drugs
- Osteoporosis
  - Bone building drugs, soy products, weight-bearing exercise
- Vaginal dryness
  - Vaginal lubrications, vaginal estrogen, flax seed oil, black cohosh
- Mood changes / depression
  - Antidepressants, exercise, St. John's Wort
- Heart disease
  - Healthy diet, exercise, cholesterol lowering drugs

JAM

Skeletal

Arthritis

COX 2 inhibitors
- Celecoxib (Celebrex) - AS new indication
- Infliximab (Remicade) – blocks TNF
  - Given in combination with methotrexate
  - Given in rheumatolgist office by IV infusion
  - Contraindicated in TB
  - Also indicated in Crohn's disease
- Adalimumab (Humira) – blocks TNF
  - Given by injection every other week at home
  - Given with or without methotrexate or other DMARDs
- Etanercept (Enbrel) – blocks TNF
- Certoliizumab (Cimzia) – blocks TNF
- (Arava)
- Anakinra (Kineret) – blocks protein interleukin-1
- Abatacept (Orencia) – prevents T cell activation
- Rituximab (Rituxan) – depletes B cells
- Hydroxychloroquine (Plaquenil)

JAM

Ibuprofen & Famotidine

- Indicated – treatment of osteoarthritis and rheumatoid arthritis to reduce risks of GI ulcers
- Dose forms – 800mg/26.6mg
- Combination of #1 NSAID with gastroprotective therapy
- Available as - ***Duexis***

Diabetes Mellitus (DM)

- Hyperglycemia caused by metabolic disorders, with Type I and Type II replacing terms insulin dependent (IDDM) and non insulin dependent (NIDDM)
  - Type I – insulin deficiency and tendency to develop ketosis
  - Type II – heterogeneous group characterized by variable degree of insulin resistance, impaired insulin secretion, and increased glucose production. Other types include endocrinopathies (Cushing's, pheochromocytoma, hyperthyroidism, acromegaly), drugs (corticosteroids) and pregnancy
- 27% increase in DM from 1998-2002 (6.5% of pop.)

JAM

Diabetes Mellitus (DM)

- Diagnosis of DM
  - *Fasting glucose >126mg/dl*
  - Symptoms of diabetes and a random blood glucose of >200mg/dl after a 75g oral glucose tolerance test
- Intermediate categories ("Prediabetes") – not DM but at substantial risk of developing type II DM and cardiovascular disease in the future
  - *Impaired fasting glucose (IFG) - (100-126mg/dl) or HA1c of 5.7*
  - *Impaired glucose tolerance (IGT) – (140-200mg/dl)*
- Screening with fasting blood glucose – every 3 years >45years, or sooner if additional risk factors

JAM

Risk Factors for Type II DM

- Family history of DM
- Obesity (>20% desired body weight)
- Age >45years
- Race / ethnicity – ex. African American, Hispanic, Native American, Asian, American, Pacific Islander
- Previous identified IFG or IGT
- History of GDM or delivery of baby >9lbs
- HTN
- HDL <35mg/dl and/or TG>250mg/dl
- Polycystic ovary syndrome

JAM

Treatment - Diabetes Mellitus

- Education, control of multisystem complications
- Target HbA1c <7.0% *(trending lower to 6.0-6.6%)*
- Type I DM require 1.0U/kg/D insulin divided into multiple doses, typically combining intermediate and short acting insulins, given before morning and evening meals or continuous subcutaneous insulin infusion device
- Type II DM controlled with diet and exercise alone or in combination with oral agents, insulin or combinations of oral and insulin.

JAM

Treatment - Diabetes Mellitus

- A sulfonylurea or metformin as initial therapy is reasonable because of efficacy, low side effects and cost. Metformin lowers insulin resistance, reduces weight, improve lipid profiles and does not cause hypoglycemia with monotherapy. Combinations of 2 oral agents have additive effects with stepwise addition of bedtime insulin or 3rd oral agent if needed. Insulin as in Type I when needed. If >1U/kg/D is needed, consider combination therapy with thiazolidinediones or metformin
- Morbidity and mortality can be greatly reduced by timely and consistent surveillance procedures

JAM

Oral Drugs For DM

- Sulfonylureas - 1st generation
  - Acetohexamide (Dymelor)
  - Chlorpropamide (Diabenese)
  - Tolazamide (Tolinase)
  - Tolbutamide (Orinase)
- Sulfonylureas - 2nd generation
  - Glimepiride (Amaryl)
  - Glipizide (Glucotrol)
  - Glyburide (DiaBeta / Micronase / Glynase)

JAM

Oral Drugs For "Prediabetes"

- Alpha - Glucosidase Inhibitor
  - Acarbose (Precose)
  - N=1429 X 3yrs, developed DM 42%, with Acarbose 32%
- Biguanide
  - Metformin (Glucophage)
  - N=3234 X 4yrs, brisk walking 2.5hrs/wk, lose weight, less fat intake reduced risk by 58%
  - Reduced risk of DM by 31%
- New Combination Therapy
  - Glipizide/Glucotrol & Metformin/Glucophage (Metaglip)

JAM

Drugs For DM

- Insulin Preparations
  - Short acting
    - Regular
    - Lispro Insulin (Humalog)
  - Intermediate acting
    - NPH
    - Lente
  - Long acting
    - Ultralente
    - Glargine

JAM

Drugs For DM

- Combination Insulin Preparations
  - 75/25-75%
    - NPH, 25% regular
  - 70-30-70%
    - NPH, 30% regular
  - 50/50-50%
    - NPH, 50% regular
  - Strategy is to exploit different onset of actions, peak of actions, and effective/maximum durations of actions by combining products

JAM

Insulin Sensitizing Agents - DM

- Thiazolidinedione – these new insulin sensitizing drugs allow dosages of insulin to be decreased and combination therapy with oral agents to achieve better glycemic control in pts with HA1c >8, on >30U of insulin/day
  - Troglitazone (Rezulin)
  - Rosiglitazone (Avandia) *
  - Pioglitazone (Actos) *
  - Repaglinide (Prandin)
- New combination – Avandaryl qd
  - Rosiglitazone (Avandia) & Glimepiride (Amaryl)

JAM

Guidelines for Ongoing Care of DM

- Self monitoring of blood glucose
- HbA1c testing 2-4 times per year
  - Each 10% decrease in HA1c = 39% reduction in progression of retinopathy
- Patient education
- Nutrition education
- Eye examination – annual
- Foot examination – annual
- Screening for diabetic nephropathy (urine albumin)
- Blood pressure – quarterly
- Lipid profile - annual

JAM

Metformin as Initial Oral Therapy

- 11 drug classes available as initial monotherapy for type 2 DM with vast choice of therapeutic mechanisms, costs and side effects
- Dispite guidelines recommending metformin as initial drug of choice, 57.8% of individuals began treatment with metformin
- Beginning with metformin was associated with reduced subsequent treatment intensification, without differences in rates of hypoglycemia or other adverse effects
- JAMA Intern Med 2014;174(2) 1955

JAM

"Artificial Pancreas" for DM

- Paradigm system (Medtronic) – combination insulin pump and glucose monitoring system
  - Helps type 1 diabetics to avoid dangerous episodes of hypoglycemia, reduce risks of death
  - Worn like a pager taped to the abdomen, continuously reads blood sugar transmits data to pump which beeps or vibrates if sugar drops to dangerous levels
    - Avoids "dead in the bed syndrome" in young
  - Eliminates need for needle use to administer or test sugar levels
  - $7,000. cost

JAM

Future Directions

- Insulin Eye Drops *****
- Insulin nasal sprays – Exubera (Sanofi & Pfizer)
- Diabetic Retinopathy Treatment – DRS & ETDRS established photocoagulation as standard of care for retinopathy since 1974, BUT….
  - Fluocinolone acetonide implant (Envision TD/B&L)
  - Vascular endothelial growth factor (VEGF) studies in PDR and ARMD
    - Lucentis (Genentech)
    - Macugen (Pfizer)
- DPP-4 inhibitors – new class of diabetes medications
  - Januvia (Merck) - type 2 DM highly effective !!
  - Galvus (Novartis) – (phase 3)

JAM

Saxagliptin

- Indicated – treatment of adults to improve control of Type 2 DM
- Dose – one daily (weight neutral)
- Significant reductions in HA1c partnered with oral anti-diabetic agents
- Available as - ***Onglyza***

Saxagliptin / Metformin

- Indicated – treatment of adults to improve control of Type 2 DM
- First and only daily metformin & DPP-4 inhibitor combination
- Dose – one daily (weight neutral)
- Significant reductions in HA1c partnered with oral anti-diabetic agents
- Available as - ***CombiglyzeXR***

Liraglutide

- Indicated – treatment of adults to improve glycemic control in type 2 DM
- Gut – slows gastric emptying
- Liver - lowers glucose output
- Pancreas – improves insulin secretion
- Significant reductions in HA1c partnered with oral anti-diabetic agents
- Available as - ***Victoza***

Linagliptin

- Indicated – treatment of adults to improve glycemic control in type 2 DM
- Only DPP-4 inhibitor at one dose for adults
- Significant reductions in HA1c partnered with oral anti-diabetic agents
- Not for use with insulin
- Available as - ***Tradjenta***

Dapaglifozin

- Indicated – treatment of type 2 DM
- Sodium glucose co-transporter inhibitor
- Dose – 5mg once daily
- SE – UTIs
- Available as - ***Farxiga***

Dulaglutide Injection

- Indicated – treatment of type 2 DM, not a first line Rx
- Helps body release more of its own insulin, but not a substitute for insulin injections
- May lose weight, improves A1C and blood sugar numbers
- Dose – injection pen; 0.75mg/0.5ml, 1.5mg/0.5ml ***once weekly***
- SE – nausea, vomiting, diarrhea, decreased appetite, pancreatits, kidney failure
- Available as - ***Trulicity***

Insulin Glargine Injection

- Indicated – adults w DM
- Long acting beyond 24 hrs with stable levels
- No peaks or wear-off betw doses
- Significant reductions in HA1c
- 3 times as much insulin in 1ml compared with standard insulin
- Not for use w alcohol
- Available as - ***Toujeo***

Empagliflozin

- Indicated – treatment of adults to improve glycemic control in type 2 DM
- Significant reductions in HA1c partnered with oral anti-diabetic agents
- Not for use with Type 1
- SE – yeast infections of penus, vagina, dehydration
- Available as – ***Jardiance***
- ***Jardiance & Tradgenta combination - Glyxambi***

Empagliflozin / Linagliptin

- Indicated – treatment of adults to improve glycemic control in type 2 DM
- First in class medication simultaneously inhibit 2 proven targets – SGLT2 & DPP-4
- Not for use with Type 1
- Contraindicated in kidney failure
- SE – yeast infections of penus, vagina, dehydration and importantly pancreatits
- Available as - ***Glyxambi***

Lorcaserin (Arena Pharm)

- Indicated – treatment of obesity & overweight patients with one related health problem (HTN, DM, cholesterol)
  - Obesity >30 BMI, Overweight >27 BMI
- Approved 2012
- Prescribed with reduced calorie diet & exercise program
- SE: "serotonin syndrome"-produce excess serotonin, agitation, diarrhea, sweating, fever, spasms, mental changes
  - Antidepressants and migraine medications additive to these SE
  - No heart valve problems
- Available as – ***Belviq***

Phentermine / Topiramate (Vivus, Inc)

- Indicated – treatment of obesity & overweight patients with one related health problem (HTN, DM, cholesterol)
  - Obesity >30 BMI, Overweight >27 BMI
- Approved 7/18/12
- Prescribed with reduced calorie diet & exercise program
- SE – tingling of hands/feet, constipation, insomnia, taste perversion, dry mouth
- Contraindications – glaucoma, hyperthyroidism, recent heart disease, stroke
- Available as – ***Qsymia (3.75/23, 7.5/46, 11.25/69, 15/92)***

Phentermine / Topiramate (Vivus, Inc)

- 2 clinical studies confirmed benefit
- One year results = 7-9% weight loss
- 62-69% = 5% weight loss
- Safety concerns?
  - ***Phentermine was half of fenfluramine (Fen-Phen) linked to heart valve damage and taken off market 1997***
  - ***13 billion settlement***

Emtricitabine / Rilpivirine / Tenofir

- 1st complete regimen for HIV infection
- Indicated – HIV infection in treatment naïve patients
- Contraindicated – in HIV with co-infection wth HBV
- Available as - ***Complera***

Emtricitabine / Cobicistat / Tenovir

- Complete regimen for HIV infection
- Indicated – HIV infection in treatment naïve patients
- Contraindicated – in HIV with co-infection wth HBV
- Dose - qd
- Available as - ***Stribild***

Raltegravir

- Indicated – HIV infection in combination with other antiretroviral agents
  - Use of other agents concomitantly increases response
- Dose – qd
- SE – insomnia, HA, nausea, fatigue
- Available as - ***ISENTRESS***

Darunavir (Prezista) & Cobicistat (Tybost)

- Indicated – HIV infection in adults
- Dose – qd
- SE – insomnia, HA, nausea, fatigue
- Available as - ***Prezcobix***

Old NRTIs for Macular Degeneration

- Indicated – HIV infection includes AZT and 3 others
- Block enzyme and a collection of proteinsvirus uses to make copies and blocks pathway for activating inflammatory processes
  - Proven to help in AMD & GVH disease
  - Proven in mice AMD as well as human retinal cells in the lab
- Science 2014 Ambati, J Univ Kentucky
  - Clinical trials to begin and will take 2-3 years
  - Already FDA approved and inexpensive to repurpose

Alternative & Complimentary Medicine

- Tumeric (curcumin) – key ingredient in curries and Indian food for centuries
  - Promising for cancer (colorectal, pancreatic, multiple myloma), psoriasis and Alzheimer's (UCLA 4gm dose/day = 120 curry dinners)
  - Inexpensive, widely available, anti-inflammatory (COX-2), antioxidant
  - J&J sells tumeric Band-Aids in India

JAM

Thank you

JAM

pellevé®

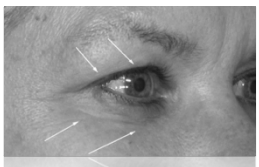
Non-invasive periorbital skin rejuvenation

Richard E. Castillo, OD, DO
Kathleen F. Elliott, OD., Dipl. ABO

FINANCIAL DISCLOSURE

Neither Dr. Elliott nor Dr. Castillo have any financial interests or professional relationships with the manufacturer(s) of any commercial product(s) discussed in this educational presentation including grant/research support, employment, consulting and/or speakers bureau arrangements, or major stock ownership.

Introducing:
Office-based Radiofrequency (RF) Skin Rejuvenation!



Dermatochalasis
(Skin touching upper lid lashes)

Normal lid crease restored
(Skin off lashes following *Pellevé* RF treatment)

Key Points…

- Nonsurgical rejuvenation of the periorbital skin produces a profound improvement in overall facial appearance.
- It can reduce, or reverse the morbidity induced by facial aging and its pathological correlates:
  - skin laxity (dermatochalasis)
  - lid malposition (senile entropion)
  - poor lid/globe apposition mechanics
    - corneal wetting
    - dry eye symptoms
    - contact lens intolerance
  - visual field restrictions
  - decreased visual acuity

5

Understanding the Aging Face

- Aging contributes to:
  - Collagen and elastin loss
    - Loss of skin elasticity
    - Thinning of dermis (volume loss)
    - Wrinkles
    - Skin redundancy and laxity (e.g., around the eyes)
  - Sun damage
    - Texture changes
    - Veins
    - Redness
    - Age spots
  - Fat Atrophy
    - Loss of volume
    - Most noticeable around eyes, cheeks, temples, lips and around mouth.

Key Points…

- Facial aging is characterized by volume loss from multiple tissue planes
  - bone
  - muscle
  - subcutaneous fat
  - skin
    - dermis
    - epidermis
- This volume loss coupled with loss of skin elasticity, actinic damage and gravity results in the "aging face."

Key Points…

- Periorbital aging changes result from multi-planar volume loss from the skin of the:
  - eyelids
  - periorbita
  - brow regions
- Identification, and treatment of age-related tissue volume loss is essential for the effective maintenance or restoration of the functional integrity of these tissues.

Lower lid skin laxity

Post-treatment

Key Points…

- Since volume loss is a cardinal feature of aging, adoption of a **predominantly volumetric** rather than an ablative approach to the periorbital skin may yield the best results.
- Radiofrequency technology offers a noninvasive approach to tissue volume augmentation.

Key Points…

- Skin rejuvenation using monopolar radiofrequency (RF) treatment is used by physicians and trained technicians to promote tissue tightening, dermal augmentation, wrinkle reduction, and tissue contouring.
  - Rusciani A, Curinga G. Nonsurgical tightening of skin laxity: a new radiofrequency approach. *J Drugs Dermatol.* 2007 Apr;6(4):381-6.

J Drugs Dermatol. 2007 Apr;6(4):381-6.

Nonsurgical tightening of skin laxity: a new radiofrequency approach.

Rusciani A[1], Curinga G, Menichini G, Alfano C, Rusciani L

Author information

1Division of Dermatology, Plastic and Reconstructive Surgery, University of Rome "La Sapienza", Italy. skinlaser@skinlaser.it

Abstract

BACKGROUND:

Improvement in skin laxity can be difficult to achieve without invasive surgical procedures. Monopolar radiofrequency (RF) treatment is used by physicians to heat skin and promote tissue tightening and contouring. RF technology produces an electric current that generates heat through resistance in the dermis and subcutaneous tissue. The thermal effect depends on the conductivity features of the treated tissue. When heated, collagen fibrils will denature and contract, which is believed to lead to the observed tissue tightening.

METHODS:

Ninety-three consecutive patients with mild to moderate laxity were included in the study. The Surgitron Dual Frequency RF (Radiowave technology, Elman International) was used to treat skin laxity. The application of RF energy took place in an ambulatory setting with no need for skin sterilization or anesthesia.

RESULTS:

Patients immediately noticed a microlifting retraction in the treated tissues according to the vectors mapped in the area. There were no significant complications and the majority of patients were satisfied with the procedure and able to return to their daily routine after leaving the office, thereby substantiating the popularity of noninvasive rejuvenating procedures.

PMID: 17668535 [PubMed - indexed for MEDLINE]

Key Points…

- Evidence in the literature supports the scientific mechanism of action as acute collagen modification and continued neocollagenesis resulting in increased dermal volume.
  - Taub AF(1), Tucker RD, Palange A. Facial tightening with an advanced 4-MHz monopolar radiofrequency device. *J Drugs Dermatol.* 2012 Nov;11(11): 1288-94.

J Drugs Dermatol. 2012 Nov;11(11):1288-94.
Facial tightening with an advanced 4-MHz monopolar radiofrequency device.
Taub AF(1), Tucker RD, Palange A.
Author information

Abstract
BACKGROUND:
Over the past 10 years, radiofrequency (RF) technology has been utilized for nonablative treatments for the treatment of stylides and skin laxity. This manuscript reviews the scientific background of collagen synthesis in vivo and in response to RF energy as well as a clinical study of 17 patients receiving a series of facial treatments with a 4-MHz monopolar RF (Pellevé, Ellman International, Inc, Oceanside, NY). Clinical methods, results, and a review of the literature for RF aesthetic treatments of the face are presented.
METHODS:
Seventeen patients were treated in one site with 6 total treatments scheduled as follows: 1 session was performed every 15 days for 2 consecutive sessions, 1 session every month for 2 consecutive sessions, and 1 session every 2 months for 2 consecutive sessions. Both the treating physician and the patients via live viewing and comparison with baseline photographs performed assessment of results. Results are reported as averages across the 17 patients.
RESULTS:
Two weeks after the first treatment, patients noted an overall average of 25% to 30% improvement. Just before the last or sixth treatment, there was an average of 50% improvement noted by the physician, with patients ranking an average self-improvement of 48%. The treating physician rated average improvement of 46% compared with baseline, whereas the patients ranked average improvement of 50% in comparison to baseline at 1 year after treatment was completed (6 months after the final treatment). Patients find this treatment to be very well tolerated, with minimal to no discomfort and no downtime or significant side effects.
CONCLUSIONS:
The Pellevé 4-MHz monopolar RF device is effective, safe, and very well tolerated for treating laxity, texture, and wrinkles of the skin without complication or discomfort. Evidence in the literature supports the scientific mechanism of action of acute collagen modification and continued neocollagenesis observed with the system. In this cohort, patients maintain approximately 50% improvement on average at 6 months and a 30% to 50% improvement 1 year after beginning the treatments, 6 months after completion.
PMID: 23135076 [PubMed - indexed for MEDLINE]

Key Points…

- The Pellevé® (*Ellman, Inc.*, Hicksville, NY) 4-MHz monopolar RF device is effective, **safe, and very well tolerated** for treating laxity and wrinkles of the periorbital skin without complication or discomfort.
  - Taub AF, Tucker RD, Palange A. Facial tightening with an advanced 4-MHz monopolar radiofrequency device. J Drugs Dermatol. 2012 Nov;11(11):1288-94.
- Volumetric rejuvenation of the periorbital skin is an important element/adjunct in maintaining and restoring normal periocular and eyelid function, appearance, and their physiological and functional correlates:
  - the function of the lids and lacrimal apparatus
  - the tear film and corneal integrity
  - the functional visual decline experienced with dysfunctional lid/lacrimal mechanics.

Pellevé® is a registered trademark of Ellman International, Inc., Hicksville, NY

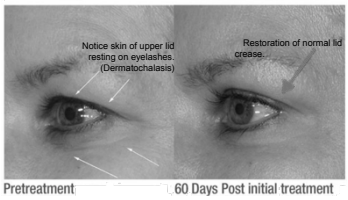
Pellevé® Skin Rejuvenation System

- Reduces skin laxity (e.g, dermatochalasis).
- Reduces facial wrinkles (e.g., periorbital rhytids).
- **No down time – immediate return to normal activity**
- **Minimal discomfort**
- **No anesthetic or skin cooling required**
- "*Research clearly demonstrates the power of the Pellevé Wrinkle Reduction System. With a single Pellevé treatment, over 87% of our patients experienced an improvement in skin laxity and fewer overall facial wrinkles at six months. The Pellevé Wrinkle Reduction System is an effective, non-invasive, economical and safe tool.*"

Dr. Antonio Rusciani
Division of Dermatology, Plastic and Reconstructive Surgery, University of Rome, Italy.

The Pellevé® System for the reduction of dermatochalasis and upper lid hooding

Aging changes in the skin are associated with:
- Loss of collagen
- Loss of elastin
- Thinning of dermis
- Thinning of epidermis
- Sagging of skin
- Wrinkles
- Ocular rhytids
- Age-related Dermatochalasis or skin laxity



Pretreatment — 60 Days Post initial treatment

Radiofrequency rejuvenation:
- Induces new collagen deposition
- Induces new elastin deposition
- Adds volume to the dermis
- Tightens and firms the skin
- Reduces wrinkles

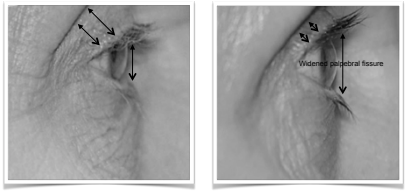
BEFORE and AFTER
Reduction of lower lid skin laxity following a single Pellevé® treatment

Aging changes in the skin are associated with:
- Loss of collagen
- Loss of elastin
- Thinning of dermis
- Thinning of epidermis
- Sagging of skin
- Wrinkles
- Ocular rhytids
- Age-related Dermatochalasis or skin laxity

Pretreatment — 180 Days Post-treatment

Radiofrequency rejuvenation:
- Induces new collagen deposition
- Induces new elastin deposition
- Adds volume to the dermis
- Tightens and firms the skin
- Reduces wrinkles

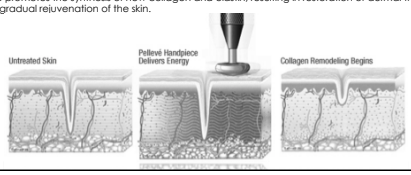
Notice **significant** improvement in the position of the superior lid margin



Pre-Pellevé™ Treatment — Post-Pellevé™ Treatment

How does Pellevé work?

- The Pellevé device precisely delivers energy into the dermis using patented radiofrequency technology, inducing collagen contraction without damaging the overlying epidermis. The result is noticeable improvement in skin quality and appearance.
- Pellevé promotes the synthesis of new collagen and elastin, resulting in restoration of dermal thickness and a gradual rejuvenation of the skin.

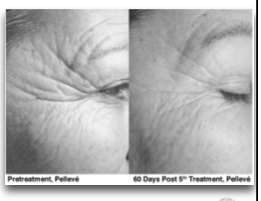


Wrinkle Reduction Animation Model with Radiofrequency

pellevé
Elegance through science

Pellevé Q & A

- How long does the procedure take?
  - A full facial treatment can be performed in about 30 minutes. The periorbital region can be done in around 10 minutes.
- Are there any immediate after-effects?
  - Mild swelling and redness may occur, but studies have demonstrated that this usually goes away within 2 to 24 hours.
- How long does it take to see results?
  - Many patients see results immediately even after the first treatment. Continued improvement may be seen for up to 6 months while the skin produces new collagen. Continued treatments tend to improve results.
- How much does a treatment cost?
  - Depending on how many areas of the face are being treated, providers are charging between $500 to $2,500 per session.



How long does Pellevé last?

A 200 study by Rusciani A, Curinga G, Merlichini G,rrAllano C, Rusciani L. Nonsurgical tightening of skin laxity: A new radiofrequency approach.

- 93 patients followed for 6 months after a single treatment
- Three independent, blinded assessors [2 facial plastic surgeons & 1 dermatologic surgeon] rated improvement over baseline for each time frame
- Response defined as average rating of three assessors indicating greater than 25% improvement in depth and number of wrinkles and improvement in tightness of the skin

A maintenance treatment is typically recommended once every 6 months.

21

Oklahoma
Board Of Examiners In Optometry

Statute 581 dealing with scope practice definition:

Correcting ocular abnormalities .....excluding cosmetic lid surgery.

22

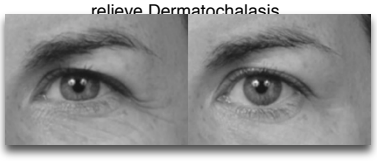
Oklahoma
Board Of Examiners In Optometry

The Oklahoma Board of Examiners in Optometry has determined that ***Pellevé*** ® is not a cosmetic procedure if it is used in accordance with the intent of the law to relieve ocular abnormalities.

23

Oklahoma
Board Of Examiners In Optometry

Pellevé ® can be used in the ocular adnexa to relieve Dermatochalasis



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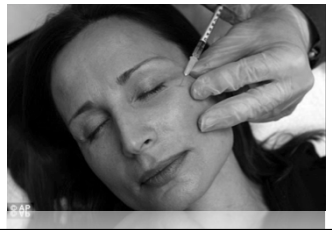
Women would like an alternative to this:



25

26

And they don't want to look like this:

27

And they definitely don't want this:

28

Acyclovir prophylaxis?

29

- The loss of collagen causes skin to droop and fall where the collagen used to keep it in place.
- ***Pellevé***® will appeal to patients in their mid-30's!

30

- Patients can go back to work immediately right after treatment with no downtime.
- Patients can use their normal facial regimen for:
  - cleaning
  - make-up
  - lotions (e.g., Retin-A)

31

- Safest anti-aging tool for women of colour:
  - African American
  - Native American
  - Hispanic

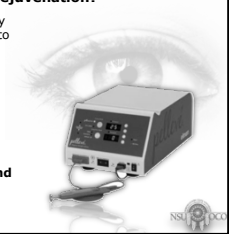
32

- Is it better than Botox with needles or the CO2 laser?
- It is less invasive and less drastic than the CO2 laser leaving you with a more natural look immediately after treatment.

Post-CO2 Laser Surface Ablation

In Summary: **Why *radiofrequency* skin rejuvenation?**

- Medical studies have proven that radiofrequency skin rejuvenation is a **safe and effective** way to treat skin laxity and minimize wrinkles without surgery.
- The side effects and discomfort are minimal to nonexistent.
- **No drugs or anesthesia** are used.
- **No down time**. Patients can return to work immediately following the procedure.
- **Allows you to treat the pathological and functional periocular correlates to aging and skin laxity AND achieve a simultaneous cosmetic benefit for your patient!**



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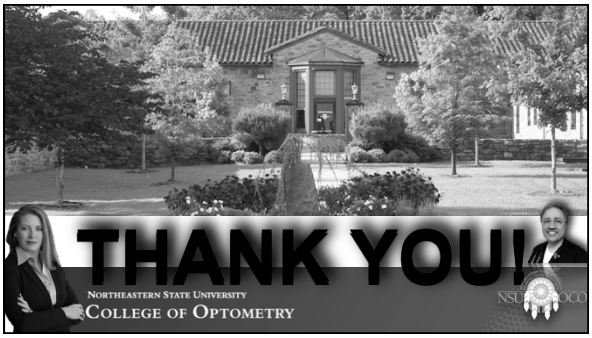

New Tools for the Toolbox

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
- McGreal Educational Institute
- ODExcellence
- 11710 Old Ballas Rd.
- St. Louis, MO. 63141
- 314.569.2020
- 314.569.1596 FAX
- mcgrealjohn@gmail.com

JAM

New Era in Refractive Surgery

- Optimization – continuous improvement of a technique or technology
- Goals of a better procedure
  - Cornea remains intact
  - Flap-less / minimally invasive
  - Single system / no patient relocation
  - Less denervation / dry eye
  - Predictability

JAM

ReLEx SMILE Procedure / Zeiss

- Small Incision Lenticule Extraction
- Micro-Invasive refractive surgery is here
- Paradigm shift is COMING
- Combines femto-second laser technology
  - VisuMax/Zeiss
  - Creates thin disc of tissue inside intact cornea
- Precise lenticule extraction through small incision
- 80,000 eyes worldwide (China, Asia, Europe)
- Single surgery
- No excimer

JAM

ReLEx SMILE Procedure / Zeiss

- Benefits to patients and surgeons
  - Cornea remains intact
  - Cap incision is 80% shorter (20mm now is 4mm)
  - Far less dry eye
  - No flap related complications
  - Single system and no relocation of patient
- USA clinical trials now treated 255 patients
  - 1-8 D / 22-54 yrs / -5.00D average
  - 100% 20/20 or better / no scatter of results
  - 90% within 0.25D at one week / MRSE = +0.02D
  - Look better / See better / feel better than LASIK fellow eye

JAM

Corneal Inlays

- Trying to create surgical alternative to monovision and multifocal contact lenses
- "modified monovision"- won't correct above -2D
  - 1.50D best
- Can use spectacles for distance and stereo-binocularity
- Placed in Pocket under LASIK flap
- Creates depth of focus & Improves reading vision
- Less distance in operative eye
- Ease of removal, exchange, repositioning
- Loss of contrast sensitivity

JAM

Effective Presbysurgery

- Must be extraocular
- Must preserve distance quality vision
- Must provide improved functioning at intermediate and near
- Should not require perpetual enhancement or revision
- Must be reversible
- Pocket techniques are viewed as superior in cornea inlay surgery as they maintain structural integrity, avoid issues of flap striation, preserve corneal nerve health, allow quicker healing

JAM

Corneal Inlays

- KAMRA (AcuFocus, Irvine CA)
  - Creates pinhole effect with 1.6mm pupil
  - Benefit – good distance is preserved OU
  - Good continuous range of vision at near
  - Decrease in night vision
  - Placed in pocket at 400um depth under LASIK flap
- Raindrop (Revision Optics, Lake Forest CA)
  - Creates depth of focus
  - Less distance vision but better near
  - Loss of contrast sensitivity, Halos at night but regain after 1 year
  - Placed directly under LASIK flap
  -

JAM

Scleral Implants for Presbyopia

- VisAbility Implant (Refocus Group, Dallas TX)
  - 4 small clear plastic implants
  - Inserted below scleral surface
  - Vaulting of sclera lifts underlying ciliary muscle

JAM

Technis MF IOLs / Abbott Medical, IL

- Available now in 3 platforms to customize according to patients needs
- Technis MF IOL +2.75D
  - Best for intermediate vision needs, and has 97% satisfaction
- Technis MF IOL +3.25D
  - Best for longer reading distances
- Technis MF IOL + 4.0D
  - Best for those requiring near vision, reading, sewing
- Offers opportunity to mix these for unique customization
- Our plan is +4.0D in non-dominant eye and +2.75D in dominant eye

JAM

Emerging Surgery Options for Presbyopia

- Extended Depth of Focus IOLs
  - Redistribute light rays to extend single focus in monofocal IOL to a range of foci
  - Create spherical aberration that increases depth of focus
  - Extension of multifocality with compensation of chromatic aberration to offset loss of contrast sensitivity
  - One focal point spread over 2D+ range
  - Can exploit “micromonovision” by being off 0.50D and be within 2D range so still keep 20/20 but read well
  - Clinical trials demonstrate 98% patient satisfaction
- Coming soon TechnisSymphony/AMO, Mplus/Oculentis, MiniWell/SifiMedtech, IC-8IOL/AcuFocus

JAM

Technis Symphony / Abbott Medical, IL

- Extended Depth of Focus IOL about 1 year away from FDA approval
- Unilateral or bilateral, with or without astigmatism
- One piece acrylic design same as TechnisMF
- Diffractive echelette but ONE image on retina not 2 like other MFIOLs
- No glare or halo (similar numbers to monofocal IOLs)
- 20/25 @near 46%, @intermediate 91%, @distance 95%
- 20/40 @near 88%, @intermediate 99%, @distance 99%

JAM

Tomorrow's Best IOLs

- Calhoun Vision, Inc.
  - Next generation *"adjustable"* material, unique, unstable, silicone, foldable
    - Cross-linked silicone polymer matrix - Mechanical and optical properties
    - Macromer - Low molecular weight links to photoreactive group
    - Photoinitiator - Organic molecule dissociates into free radicals, begins polymerization on exposure to special wavelengths, moving macromer down diffusion gradient into radiation area thickening the lens

LAL - IOLs

- 2 weeks post-operative UV protection required
- Adjust refractive error at 2 week post-op
  - Uses 380nm exposure of light at slit lamp system
- Next perform lock-in
  - Pink tint is commonly reported 1-2 days post lock-in
- Not cleared in US but Canada, Europe etc

Accommodating IOLs

- Sapphire AutoFocus IOL (Elenza, Roanoke VA)
  - Electro-optic diffractive IOL - Monofocal IOL with central aspheric modification
    - Far & intermediate vision
  - Smart electro active diffractive liquid crystal
    - Near
    - Microsensors detect physiologic triggers of accommodation, pupil size change and illumination decrease
    - Onboard processors & algorithms to control power sequence by altering index of refraction of the material
    - Lithium ion power cells – weekly charge

Accommodating IOLs

- AkkoLens (AKKOLens International)
  - Sulcus implants
  - 2 lenses moving perpendicular to optical axis with ciliary body movement
  - Move in opposite directions
  - Lenses have variable curvatures to increase accommodative power up to 6D
- Nulens (Nulens LTD, Israel)
  - Sulcus implant
  - Counterintuitive mechanism

Accommodating IOLs

- Fluid-Vision Lens (Power Vision, Belmont CA)
  - Annular 3-D haptics communicate with center optic
  - All filled with silicone oil
  - Oil moves in and out of optic changing its power
  - Optic outer shell is proprietary hydrophobic acrylic
  - Inside is index matched silicone oil so no interface optical issues
  - Minimum of 2-2.5D accommodation, 3-5D average (35yr old)
- Triplet – sandwich of 2 convex lenses and a concave lens in the middle: produces up to 6 D accommodation
  - Different materials and different index of refraction
  - Compression by ciliary body of 1um = 1D accommodation

Argus II / Second Sight Medical/USC

- Creating the bionic eye for retinitis pigmentosa
- Approved by FDA on Feb 14, 2014 as humanitarian use device (affecting <4000/yr)
- US Dept of Energy, National Eye Institute at NIH and National Science Foundation collaborated and provided grant funding over $100 million to support development of Argus II
- Intended to be implanted in a single eye, worse seeing
- Criteria: >25 yrs, LP or NLP intact inner retina function, past history of useful vision

JAM

Argus II / Second Sight Medical/USC

- External hardware of glasses with miniature video camera on nasal bridge transmits images via a wire to battery operated videoprocessing unit worn on the belt
- VPU transforms image into electrical stimulation delivered to a transmitting coil on side of glasses, then sent wirelessly to receiving coil sutured to sclera
- External equipment wirelessly powers the internal implant
- Internal receiving coil and electronics case secured to sclera in a buckle fashion, sent to cable through sclerotomy into eye terminating at epiretinal 60 electrode

JAM

Argus II / Second Sight Medical/USC

- Array tacked to retina-choroid-sclera
- Artificially stimulated RGCs transmit signals through axons via functioning optic nerve and tract to LGN, radiations and occipital cortex forming pixelated light images
- General anesthesia with 4 hr duration of surgery
- Post implantation device adjustments done with laptop
- Vision rehabilitation sessions - usually 5-10 for learning to use head, camera etc
- 1st important step in artificial vision for blind patients

JAM

Smartlux Portable Electronic Magnifier

- Portable CCTV, 7 oz
- Non-reflective, hard coated 5" LCD screen
- Switch between balck on white, white on black, black on yellow, yellow on black
- Magnification is 5X, 7X, 9X, 12X
- 3 screen brightness levels
- Freeze frame function, stores 20 images
- $595.00
- Eschenbach

CEPHALY / Cephaly Technologies

- Newest treatment for migraine prevention
- Headband uses low dose emission of stimulating electricity
- FDA approved > 18 years age
- Drug free, 20 minute per day
- Portable, battery operated, RX only, $300
- "counter-irritant" in CNs
- Widely used in Australia, Canada, Europe
- Studies in Belgium finds less use of drugs, significantly fewer HAs, did not eliminate Has or severity

JAM

Corneal Collagen Cross-Linking

- Progressive keratoectasia
  - progressive corneal disease
  - Refractive surgery
  - No treatment
- New treatment, old concept
  - Natural occurrence within cornea and lens
    - 4.5% increase in fibril diameter
  - Dentistry- hardens material for fillings
  - Polymer industry-hardens adhesives
  - Cardiology-glutaraldehyde hardens heart valve
  - Uses UV light & riboflavin

Collagen Cross-Linking (CXL)

- ***Riboflavin*** – photosensitizing agent
  - Excited to triple state by UV
  - Releases radicals
  - Causes hydrogen bonds between AA in collagen chains
    - At the intra & interhelical levels
    - Increases collagen diameters and spacing
- Treatment for keratoconus (1/2000, 20% need PK)
  - Pellucid marginal degeneration
  - Bullous keratopathy
  - Corneal melts/Infectious keratitis
  - LASIK ectasia

Collagen Cross-Linking (CXL)

- Contraindications
  - <400u corneal thickness (endothelia damage)
  - Incisional refractive surgery
- Procedure overview
  - Epithelial debridement (+/-)
  - Ribo 0.1% apply every 2-5 min for 30 mins
  - Exposure to UVA irradiation for 30 mins (370nm, 3mW/cm2)
  - Add ribo every 2-5 min for shielding
  - Treatment diameter 7-9mm
  - Post-op treatment same as PRK
- Results last 2-7 years, may need retreatment

Collagen Cross-Linking (CXL)

- Future applications
  - Keratoconus
  - Poor refractive surgery candidates - can now have surgery
  - Better outcomes - for good candidates for refractive surgery
  - Adjunctively in all laser refractive procedures to provide better structural support of the cornea long-term
- Not FDA cleared here yet but access is available

JAM

Ocriplasmin / ThromboGenetics, Inc

- Non surgical treatment for vitreomacular adhesions
  - Increased macular thickness
  - CME Diagnosed 8% at slit lamp 30% with OCT
- Vitrectomy vs Vitreolysis?
  - Invasive
  - Anesthesia
  - Face down
  - Retinal breaks
  - Cataract

Ocriplasmin / ThromboGenetics, Inc

- Truncated form of human plasmin produced by bacteria
- Indications: developed for dissolving blood clots in vascular disease
- Single Intravitreal injection
- Results – resolution 30% at 28 days, closure of hole 40% at 28 days
  - better than all other agents tried
- Spin offs – DME, AMD, adjunct to vitrectomy
- New England JourMed 2013
- ***Available as Jetrea***

YAG Photoablation-Vitreous Floaters

- Laser photoablation vaporizes opacities into small gas bubbles that dissolve quickly
- Indications – stable floaters x 2 mos, complete PVD, no flashes or pathology
- Strips electrons, creates a plasma, a mini nuclear reaction
- Results – 1/3rd moderate benefit to 100% depending on study; multiple treatments possible
- Wagle AM, et al Am J Ophthal 2011
  - Found symptomatic pts willing to trade 11% of remaining life and take 7% risk of blindness to get rid of floaters
- ***Available as Ultra Q Reflex / Ellex Medical Lasers LTD***

Topcon New Scanning Laser

- DRI-1 Atlantis
  - Deep range Imaging
  - Only swept source technology in OCT
- FDA approval pending
- Longer wavelength - 1,050 nm vs 850nm for SD-OCT
- Imaging speed – 100,000 A scans per second
- Swept-source will be important as we image deeper
  - Especially choroid
  - More quantitative assessments leading to databases

CANON Adaptive Optics SLO

- Adaptive optics enable precise correction for aberrations in the human eye
- Developed and AO control system that measures aberrations using wavefront sensor and controls a wavefront correction device
- Enables visualization of individual photoreceptors and blood cells
- Examination of retina at cellular level is coming soon

Cliradex

- Essential all natural effective cleanser for lashes, face and eyelids
- Indicated in blepharitis and rosacea
- Wash hands and face
- Close eye tightly
- Cool refreshing menthol sensation
- Use one side of towellete per eye
- Keep eye closed for one minute
- Biotissue.com

Cliradex

- Preservative free\essential oil
- 4-terpinol organic compound
- Melalenca aternifloria – natural tea tree oil
- Box – 24 individually wrapped towelettes per carton
- Cases of 20 cartons
- On-line purchase
- Biotissue.com

Hypochlorous acid 0.01%

- Lid hygiene product
- Rx only
- Excellent broad spectrum microbial coverage for MGD and blepharitis
- Hypochlorous acid is released by PMN white cells (neutrophils) when attacking invading organisms
- Spray a cotton round and clean lids and lashes BID
- Tested against 20 common eyelid organisms
  - Reduced numbers by 99.99% in 60 seconds
- Available as ***Avenova*** by NovaBay

MiBoThermalFlo

- Ultrathermal Therapeutic Medical Device
- Touch screen / LCD display (12in x 5in)
- Chronic dry eye treatment, 98% patient satisfaction
- Tip temp 108 degrees (manual)
- Heat element is 6w thermoelectric
- Timer is 1-16 minutes (average 12min)
- No pain or down time, warm message
- Painpointmedical.com 855.642.6356

BlephEx by RySurg

- Newest treatment for bleparitis
- In office procedure performed by doctor
- Similar design to Alger brush
  - Hand held, low torque, charger
  - Use topical anesthesia, gloves, eyeprotection/magnification
  - Consent
- Precisely eliminates scurf and bacterial debris
- Not covered by insurance
- Average cost to patient $120, repeat every3-6 months
- www.RySurg.com

JAM

Sjo Test for Sjogrens Syndrome

- Sjogrens Syndrome is common autoimmune disease affecting exocrine glands
  - 4 million in USA
  - 3 million undiagnosed!!
    - ODs are on the frontline
- Symptoms – DE, dry mouth, nose, joint pain, RA, fatigue, reflux, bronchitis, peripheral neuropathy, liver and kidney dysfunction, 5-10% lymphoma
- Diagnosis – salivary gland biopsy and biomarkers
  - 4.7 years to diagnosis

Sjo Test for Sjogrens Syndrome

Diagnosis – American College of Rheumatology (old way)

SS-A, SS-B, RF, ANA, lip Bx, vital stains of eye

40% sensitivity (changed criteria 12 Xs since 1965)

Diagnosis – Sjo Test (Nicox)

in-office blood panel test, small fingerstick collection

4 traditional markers and 3 proprietary markers

Salivary gland protein / carbonic anhydrase-6 / parotid secretory protein

90% specificity

Sjo Test for Sjogrens Syndrome

- Sjogrens Syndrome is treated early with drugs that target B-cells and TNF, typical monoclonal antibodies
- Early detection spares organs damage and improves outcomes, lowers cost burden
- Builds relationships between Optometry and primary care and rheumatology
- Sjogrens Syndrome Foundation - www.Sjogrens.org
- Nicox – www.nicox.com

Lifitegrast / Shire

- T cell modulator similar to cyclosporin but FASTER
  - Starts in 2 weeks!!
  - Phase II
- Lymphocyte function-associated antigen (LFA-1) inhibitor of intracellular adhesion molecules (ICAM-1)
- Prevents binding of T-cell mediated inflammation (LFA-1 to I-CAM-1)
- Works on ***active*** T lymphocytes
- Cyclosporin works on the ***production*** of T lymphocytes which takes 100-110 days to complete a cycle of inflammation

InflammaDry (Rapid Pathogen Screening)

- Matrix Metalloproteinase (MMP-9) is the best biomarker for ocular surface disease & dry eye
- Developed as a simple in office test to predict and prevent problems after LASIK and other surface surgery
- Also as a test for dry eye disease
- FDA reviewing now
- Will be available as ***InflammaDry***

Tear Lab

- "Lab on a Chip"
  - We have a test!
    - Analogy of treating DM without BG, HA1c etc
  - No longer needs CLIA, COLA, inspection, etc
- Gold cartridge draws nl of fluid and processes
- Osmolarity is the global marker of Dry Eye (DEWS Report)
  - Least variable test for DE
  - Central mechanism in pathogenesis of DED
  - More variable results seen in more advanced disease
  - Large differences between eyes noted, increasing with disease severity
  - 308mosmsl = Dry Eye
  - Sensitivity 72.8%/Specificty 92%
    - No other clinical sign or test is better than 62%

Tear Lab Severity Scale

- 280-300 Normal
- 300-320 Mild
- 320-340 Moderate
- 340+ Severe

Osmolarity Highest Positive Predictive Value of DED

- Osmolarity 87%
- Schirmer's 31%
- TBUT 25%
- Staining 31%
- Meniscus height 33%
- Dry Eye Workshop Report 2007 OculSurf 2007;5:2 Tomlinson A, et al IOVS. 47(10) 2006

Tear Lab

- Corneal tests and symptoms DO NOT correlate with disease
  - 30% of DE patients are ASYMPTOMATIC
  - Took 7 times for FDA to clear Restasis
  - May not see another drug
- 2007 DEWS Report - MGD most common cause of DE
  - Mucin is everywhere in the three layers of tear film
- Tear Osmolarity in Diagnosis & Management of Dry Eye, Lemp,M AmJOphth 2011;151:792-798
- Objective Approach to Dry Eye Disease Severity, Sullivan,B InvestOphthVisScience Dec 2010 Vol 51 No 12

Human Tear Serotonin Correlate with Symptoms and Signs of DE

- Many w DE describe neuropathic pain in absence of any noxious stimuli; phenotypic alterations and sensitization of peripheral nerves could occur
- Free nerve endings interdigitate between epithelial cells and are vulnerable to T cells, MMPs, interleukins, TNF
- Study support peripheral as well as central (pain) sensitization of ocular somatosensory nerves in DE
- Expands new therapeutic biomarkers and target for therapy
- Ophthal 2015;122:1675 Chhadva P et al

2Win Binocular Handheld Refractometer & Vision Analyzer

- Fully automated binocular refraction
- Operates at 1 m
- 7 second exam, no drops
- Small portable
- Battery operated
- Ideal for infants, children, disabled or non-cooperative patients
- Acoustic and light targets built in
- www.2winforvision.com 408 716 3271

DRS Digital Retinography System

- Fully automated retinal imaging
- Auto-sensing, auto-alignment, auto-focus, auto-flash adjustment
- Both eyes in one minute
- Compact clean design
- Motorized chin rest
- 40-45 degrees field of view
- Embedded PC, ethernet & Wi-Fi connectivity
- www.centerview.com Padova, Italy, Santa Clara CA

Retinoblastoma Advance

- Super-selective Ophthalmic Artery Chemotherapy as Primary Treatment of Retinoblastoma Abrams, D Ophthal 2010;117:1623
- "Chemo-surgery"
- Ophthalmic artery can be safely and repeatedly canulated in very young children
- Deliver high concentration (low dose) chemotherapy infusion on outpatient basis
- Prevents radiation, enucleation, and systemic chemotherapy

Retinoblastoma Advance

- Ophthalmic Artery Chemosurgery for Retinoblastoma Prevents New Intraocular Tumors Abramson, D Ophthal 2013;120:560-565
- New anterior tumors are found after treatment of primary tumor (XRT or chemo) in 24-48%
- OAC eyes demonstrate fewer new intraocular retinoblastomas; suggests ophthalmoscopically undetectable tumors present at initial diagnosis
- Less EUA, lower costs, higher ocular survival, less anxiety, avoidance of sided effects of repeated focal treatments

New Ideas in OCT

- Ultra-widefield with angiography
  - Extends multi-modality of Spectralis platform
  - Diseases are underestimated for lack of peripheral angiography
  - Can image out to 150 degrees
- Multi-color Imaging – Spectralis
  - High contrast, noise reduction, eye tracking
  - 3 simultaneously acquired selective color laser images
  - Versatility to view individual or multicolor images
  - Identifies pathology unclear on fundus images

Widefield Imaging Technologies

- Optos 200TX – 200 degree view or 80% of retina
  - 2 lasers off ellipsoid mirror and proprietary software
  - Images not affected by media opacities
- Spectralis/Heidelberg – add on ultrawidefield angiography module
  - Lens based system, warpage of image inherent
- Avanti / Optovue – Widefield Enface OCT
  - 40 degree field of view

Peripheral Autofluorescence in AMD

- Colin, et al Ophthal 2013;120:127-1277
- Distinct patterns of peripheral FAF abnormalities were seen in 68.9%
- AMD type correlates with Peripheral FAF changes
  - Neovascular type more common, non-neovascular type, then normals
- Age – any peripheral FAF abnormality was associated with older age
- Female patients had a higher risk of abnormal peripheral FAF compared to males

Widefield Imaging Future

- Significantly higher rate of peripheral autofluorescent abnormalities among eyes with AMD
- Both Granular fluorescent changes and patchy hypofluorescent were common in eyes with advanced AMD
- Patchy hypofluorescence was common among patients with geographic atrophy
- Peripheral pinpoint hyperfluorescecnt drusen may precede the development of more advanced disease process in the macula
- Tan et al Peripheral autofluorecence in NV AMD Opthal. 2013;12096):1271-77

Multi-Spectral Imaging (MSI)

- "virtual angiography"
- Non-invasive alternative to IVFA
- Valuable adjunct to OCT
- LEDs from 550-950u
  - Image in pairs
  - Full series is 6 flashes/12 images
  - Shorter wavelengths image inner retina layers (ex VMA)
  - Longer wavelengths image outer retina layers (ex AMD)
- Useful to gauge effects of drugs, neutraceuticals, major benefit in dry AMD

Super-dose Anti-VEGF Trial (SAVE) in AMD

- Brown, et al. Ophthal 2013;120:349-354
- Intravitreal injections of 2.0mg ranibizumab led to significant VA gains & anatomic improvements in patients with persistent intraretinal, subretinal, or subRPE fluid during a period of chronic monthly 0.5mg ranibizumab injections
- CATT demonstrated persistent fluid on OCT in 53.2% of ranibizumab & 70.9% of bevasizumab
- A significant unmet need for more potent, longer lasting or complementary mechanism of action

Anti-platelet derived growth factor in AMD

- Ophthotech Corp, NJ – anti-PDGF aptamer Fovista
- Solution to overwhelming, non-sustainable treatment burden of anti-VEGF
- ANCHOR, MARINA, CATT, HORIZON all show vision recovery for first 2-3mos, stabilizing around 4mos, then plateau for extended period with strict monthly injections
  - All demonstrate quick worsening with decreased dosing
  - Medicare claims data – fewer than 6 injections in 1st year
  - Nationwide outcomes must be worst than we want to admit!

Anti-platelet derived growth factor in AMD

- Roots of resistance – angiogenesis involves thousands of chemical factors, occurring over stages
  - Initiation/progression/differentiation/maturation/remodeling
  - Numerous cell types contribute to this growth
- Pericyctes and endothelial cell show significant "cross talk" cell signaling
- "Tip" endothelial cells blaze trails, create sprouts, secrete PDGF-B which recruits pericyctes to proliferate and migrate, protecting the endothelial cells and over time secreting more VEGF, diminishing the effect of anti-VEGF therapy

Anti-platelet derived growth factor in AMD

- Combination therapy of anti-VEGF & anti-PDGF in phase 2b demonstrate +10.6 letters improvement or 62% improvement over Lucentis monotherpy
- This appears to inhibit pericycte recruitment, strip pericytes from NV complex without negatively affecting host non-cardiovascular vessels, causing both inhibition & regression of NV complex

Pharmacogenomics & Treatment in AMD

- Currently only phenotypic/anatomic predictors of response to anti-VEGF therapy
- Technology emerging to stratify and predict responses to antiangiogenic treatments
  - Using known disease causing SNPs and haplotype odds ratios of these SNPs, drusen size, smoking history we can predict risk of progressing to advanced sight threatening AMD
- Rapidly evolving field to help individualize care and design new therapies
- In office genetic testing available soon to assess the response to AMD vitamins, down to exact ingredients

Diabetic Eye Diseases – The Next Wave

- Three Level Surge
  - Baby Boomers – 28% US population
    - AMD & DR
  - DM surge
  - Affordable Care Act (ACA)
    - Adds 32 million new covered lives
    - Many have not had proper medical care
    - Many have not had proper eye care
- "Gluttons for Punishment" – Lancet 21 July 2012, 380
  - Americans comprise 5% of world population and account for 33% obesity, overfed for first time in history, inactivity results in as many deaths as smoking

Lens Fluorescence Biomicroscope

- ClearPath DS-120 / Freedom Meditech
  - Recently approved
  - Non-invasive, biophotonic quickly detects lens autofluorescence
    - 8 seconds
    - Quantitatively
  - Confocal scanning laser reflectance microscope
  - Pupil tracker
  - Long life blue LEDs
  - Electronic transmission to EHR or other referral sources
- Eliminates fasting, blood draw, waiting time, biohazard burden

Lens Fluorescence Biomicroscope

- Screens for Elevated Advanced Glycolated End products (AGEs)
  - High correlation to uncontrolled glucose
  - Irreversible AGEs in crystalline lens
    - Benefit as a screening tool compared to HgA1c
  - Linear relationship exists between age & autofluorescence
  - Uncontrolled glucose causes deviation in the relationship
- Available in three configurations to fit any office layout

Alcon / Novartis & Google (x)

- Announced collaboration exclusive agreement to license "Smart lens" technology
  - Accommodative CLs
  - Accommodative IOLs – (1.7 Billion presbyopes)
  - Glucose sensing smart CL for Diabetes
    - Wireless connectivity to mobile device
- Google (x) special team designed driverless cars and GoogleGlass
  - "Moonshot" task team

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Amniotic Membrane Transplantation (AMT)

- Ocular surface reconstruction in SJS, severe dry eye, and severe chemical burns
- Human amniotic membrane prepared from placenta of elective cesarean section in seronegative (HIV, HepB &C, syphilis)
- Facilitates epithelialization, reduces inflammation, vascularization and scarring
- Limbal stem cell transplantation is needed in concert with AMT in the most severe chemical burns

Amniotic Membrane Transplantation (AMT)

- Acelagraft (Dehydrated Human Amniotic Membrane Allograft)
  - Highly organized matrix
  - 100% human derived
  - Non-immunogenic
- Cost
  - 1x2 $315
  - 2x3 $390
  - 4x4 $480

Promise of Implantable Drug Delivery Systems

- Humans are clumsy, forgetful, imprecise and undependable….high tech drugs are not
- Benefits - longer lasting, highly localized, accurate concentration, fewer side effects
- Reservoir implants – require surgical placement/replacement, simple, longevity, steady state
  - Retisert, Iluvien, I-vation
- Biodegradable implants – no need for removal, less toxicity
  - Ozurdex

Promise of Implantable Drug Delivery Systems

- Vitrasert – 1996 approved for CMV implant of gancyclovir, pars plana insertion
- Retisert – next generation, better target and duration, pars plana insertion and suture, good for uveitis but IOP elevations and cataract are problematic
- Iluvien – fluocinolone intravitreal implant, for AMD (wet & dry) and DME
- Ivation – treatment of DME, implantable titanium screw coated with triamcinolone, self anchors into sclera

Promise of Implantable Drug Delivery Systems – Innovations on Tap

- Biosilicone Technology – pSividia nano-structured porous silicone, bioerodable, handles any molecule size
- Replenish Media Pump – microelectromechanical device delivers continuous or bolus targeted drugs to ant/post segments via flexible cannula and refillable reservoir system (30 g needle), most of device is outside eye…"reverse-drainage glaucoma device"
- Encapsulated Cell Technology (ECT) – delivers large molecules to retina, stores complex proteins at 37degrees C without degradation

Promise of Implantable Drug Delivery Systems – Innovations on Tap

- Encapsulated Cell Technology (ECT) –
  - Genetic engineering of RPE cells via plasmid transfection
  - Plasmids encode a therapeutic protein, in to cell genome
  - Engineered cells loaded into polymer membrane capsule and inserted into vitreous
  - Continually produce the therapeutic protein
  - No need for long term drug storage
  - "makes the bread fresh daily"
  - Testing now with ciliary neurotrophic factor (CNF) in retinal disease

Promise of Implantable Drug Delivery Systems – Innovations on Tap

- Envisia – designs and manufactures micro and nanoparticles systems to deliver drugs on nanoscale
- GreyBug – micro and nanoparticle delivery systems for companies with drugs but not delivery vehicles,
- Kala Pharma – mucous penetrating particles (MPPs) to pierce mucuosal barriers providing sustain drug concentrstiononly possible before w injection or implant
- pSividia – Durasert delivery system is miniature and injectable; coming w latanoprost, fluocinolone implant, and DME drug, Tethadur system to release avastin

Ozurdex – Dexamethasone Intravitreal Implant 0.07%

- 1st & only injectable dexamethasone implant
- For non-infectious uveitis of the posterior segment
- For macular edema following BRVO or CRVO
- Solid polymer matrix biodegrades to lactic acid and glycolic acid
- Delivered by injection as in office procedure (22-gauge)
  - Ergonomically designed applicator for single use, preloaded
- Contraindicated in advanced glaucoma

Ozurdex – Dexamethasone Intravitreal Implant 0.07%

- Posterior uveitis results
  - 46.8% of treated patients had resolution of vitreous haze at 8wks
  - 42.9% gain >15 letters (3 lines) from baseline at week 8
- BRVO / CRVO
  - 9.8 letters gained at day 60
- IOP data
  - 13.9% with >10mmHg increase from baseline IOP at day 60
  - 3.2% with >35mmHg increase from baseline IOP at day 60

Rifampin as Efficacious Therapy for CSR

- Chronic Central serous chorioretinopathy is sometimes difficult to treat in a small number of patients
- No universally accepted standard exists for this macular disease
- Rifampin (Rifadin/Sanofi) – on forefront as it increases metabolism of endogenous steroids as a consequence of the inductive affect on cytochrome P450
- Promising, cost effective, efficacious therapy for CSC of 6 months duration encroaching on Macula

FAF Background Information

- Recording FAF is easy, fast & non-invasive
- FAF signals emitted across spectrum from 500-800nm
- CSLO
  - Excitation induced in blue (488nm)
  - Emission filter 500-700nm to detect
- Fundus camera
  - Excitation induced in green (535nm-580nm)
  - Emission filter in yellow-orange (615-715nm)
- Composition of images may vary between systems

JAM

FAF Signal as Predictive Marker

- Extension of abnormal FAF & FAF Pattern impact enlargement rates over time
- Serve as predictive determinants
- Find “fast progressors”
- Progression rates MORE DEPENDANT on FAF pattern than any other risk factor!!
  - Baseline atrophy size, smoking history, HTN, DM, >80yrs, family history, hyperlipidemia

JAM

AMD Research on Genetics

- Age related macular degeneration gene located
- Encodes for a protein called Compliment Factor H
  - Increases inflammatory proteins
  - Increases C-reactive protein
- We now know a genetic component of the disease exists!

SequenomCMM

- RetnaGeneAMD
  - Simple in-office DNA cheek swab
  - Tested in 1132 CNV cases and 822 controls in Caucasians
    - Multi center (Boston, Utah, Australia)
  - Results in 8-10 days
  - Genetic counseling for doctors and patients
  - Impact of 13 genetic variants (SNPs) of 8 genes on 4 chromosomes (1,6,10,19)
    - 3 SNPs increase risk
    - 10 SNPs decrease risk
- SequenomCMM – prenatal & ophthalmic
- 877.821.7266 www.sequenomCMM.com

SequenomCMM – Calculating Risk Score

- Gene
  - ARMS2 +1.45
  - CFH +0.81
  - C3 +0.42
  - F13B -0.01
  - CFHR5 -0.13
  - CFHR4 -0.15
  - CFH -0.19
  - F13B -0.45
  - CFHR5 -0.60
  - CFH -0.76
  - CFH -0.79
  - CFB -0.82
  - C2 -0.95

SequenomCMM – Calculating Risk Score

- Impact on disease
  - ARMS2 = 3.39x's increased risk
  - CFH = 2.5x's increased risk
  - C3 = 1.25x's increased risk
  - C2/FB = 0.3 protective
- Log odds established for each SNP in multiplex panel and risk scores calculated based on individual genotype assignment yielding wide spectrum of disease risk (reflective of case controlled population)
- Low risk <25% CNV probability
- High risk >75% CNV probability

What is Macula Risk Gene Test?

- Macula Risk® is a prognostic DNA test intended for patients who have a diagnosis of early or intermediate AMD.
- Using the complete combination of AMD genes, and smoking history, Macula Risk® identifies those most likely to progress to advanced AMD with vision loss.
- Macula Risk® allows you to stratify patients for appropriate monitoring as recommended by the AOA and the AAO Preferred Practice Patterns - "*in an effort to detect asymptomatic CNV at a treatable stage.*"
- The patient sample is a cheek swab taken in the doctor's office. Macula Risk® is reimbursed by most providers including Medicare.

Silence Reduces Risk of Infections

- Wills Eye Hospital study of intravitreal injections
- 126,587 IVI, retrospective case series of endophthalmitis after anti-VEGF agents
  - 48 cases / 17 culture positive
- 47,773 talking
  - 27 cases / 9 culture positive high in oral pathogens
- 78,814 no-talking
  - 21 cases / 8 culture positive
- No talking policy during IVI affective in reducing risk of infection, including oral pathogen associated cases

JAM

Pazopanib / GlaxoSmithKline

- TOPICAL
- Effect – Anti VEGF-A, targets receptor tyrosine kinase so inhibition is after VEGF binds to receptor
- Dose –5mg/ml TID
- Accumulates in high concentration in posterior retina through trans-scleral route (end around on anterior segment)
- Indication – neovascular "wet' macular degeneration
- Approved now for renal cell cancer
- Benefit – no injections, less cost, 4.3 letters at day 29 trend toward improvement at day 8

Regorafenib / Bayer

- TOPICAL
- Effect – Anti VEGF-A, targets receptor tyrosine kinase so inhibition is after VEGF binds to receptor
- Indication – neovascular "wet' macular degeneration
- Benefit – no injections, less cost,

JAM

New Wet AMD Clinical Concepts

- Ciliary Neurotrophic Factor (CNTF)
  - Immuno-isolation
  - Implanted pars plana releasing drug for over one year
  - Outer nuclear layer & photoreceptor layer thickens
    - No correlation with VA improvement
- Anti-Platelet Derived Growth Factor (PDGF)
- POT-4 / PotentiaPhama, Inc
  - Binds to C3 – Potent inhibitor of C3
  - SMALL cyclic peptide (not large 3-D protein)
    - Lasts for MONTHS!!
  - Studies using depo form combination with VEGF drugs

New Wet AMD Clinical Concepts

- Complement is MOST IMPORTANT
- Human Genome Project – completed in 2005
  - Chromosome 1 is location of complement factor H (CFH)
  - 1st to be mapped!
  - C3, C3a, C5, C5a are all pathways of activation of VEGF
- ***VEGF expression is result of complement activation!!***
  - Compliment is the bomb of inflammatory system
    - Requires detonator – 30 proteins in blood for triggers
      - Membrane Attack Complex (MAC) & Fc-Fragment

Investigational Therapy for Wet AMD

- Finding Better Anti-VEGF agents
  - ESBA (Alcon) – humanized single chain antibody fragment and pan-VEGF inhibitor
  - OSPREY – phase 2 trial of ESBA & aflibercept
  - DARPin (Allergan) – designed ankyrin repeat protein
    - Small molecule designed to bind to any receptor
    - REACH study in phase 2
- Exploring combination therapies – platelet derived growth factor, Fovista (Ophthotech) combined with anti- VEGF agents demonstrates 62% additional benefits

Investigational Therapy for Wet AMD

- Finding Better Anti-VEGF Delivery systems – 3 ways
  - Gene therapy
    - Genzyme - viral vector given intravitreally to deliver tyrosine kinase inhibitor sFLT-1, a chimeric protein that binds to VEGF
    - Avalanche – subretinal injection following vitrectomy of tyrosine kinase, phase 2
  - Encapsulated cell technology
    - Neurotech – protein factory implanted in the posterior segment, phase 3

Anti-HTN Drugs Associated with AMD

- Researchers at University of Wisconsin
  - Cohort of NEI's Beaver Dam study of 5000 residents aged 43-86
  - Use of any vasodilators was associated with 72%greater risk of developing early stage AMD
  - Use of oral beta blockers was associated with 71% increase in risk of neovascular AMD
  - *Klein et al Vasodilators, blood pressure lowering medications and AMD, Beaver Damn Study April 11, 2014 on line Ophthal*

Thank you

McGreal Educational Institute

Missouri Eye Associates

Excellence in Optometric Education

BACTERIAL CORNEAL ULCERS

Jeffrey R. Urness OD, FAAO, ABO

The light of the body is the eye: if therefore your eye is whole your body shall be full of light.
Matthew 6:22

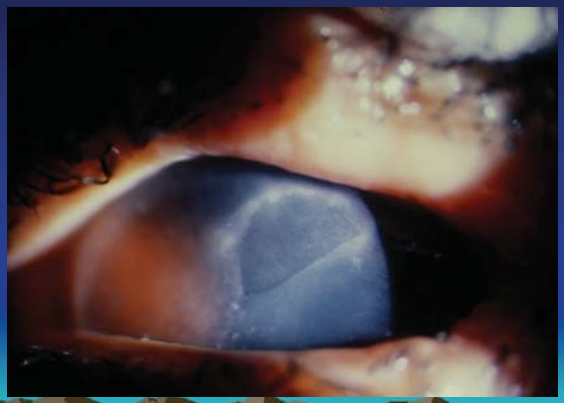
INFECTIOUS CORNEAL ULCERS

- ONE OF THE MOST SERIOUS CONDITIONS FACED BY EYE CARE PROVIDERS
- A TRUE OCULAR URGENCY
- IS IT INFECTIOUS KERATITIS OR INFECTIOUS ULCER OR BOTH

IS IT REALLY AN INFECTIOUS ULCER?

- ABRASION – CAN HAVE HAZE; NO INFILTRATE
- ABRASION OVER SCAR - GRAM STAIN SHOWS FEW OR NO PMNs
- ULCER – INFILTRATE / GRAM STAIN SHOWS LOTS OF PMNs

CORNEAL ABRASION



DIFFERENTIAL ETIOLOGIES

- BACTERIA
- FUNGUS
- UNUSUAL ORGANISMS
- HERPES

HISTORY

- BACTERIAL – RAPID ONSET WITH PAIN WORSENING HOUR BY HOUR
- FUNGAL – INJURY BY ORGANIC MATTER; CL WEAR; ONSET OVER SEVERAL DAYS; DISPROPORTIONATE PAIN +/ -- ; IMMUNOCOMPROMISED
- ACANTHAMOEBA – EXPOSURE TO CONTAMINATED WATER, SOLUTIONS OR SOILS. DISPROPORTIONATE PAIN, THOUGH NOT IN ALL CASES
- NEUROTROPHY; LESSER, DIFFERENT PAIN
- CAN HAVE COMBINED ORGANISM INFECTIONS

BACTERIAL ULCERS CLINICAL FEATURES

- EPITHELIAL DEFECT – 99%
- INFILTRATE
- STROMAL NECROSIS
- ATTACHED MUCOPURULENT MATERIAL
- A.C. REACTION / HYPOPYON

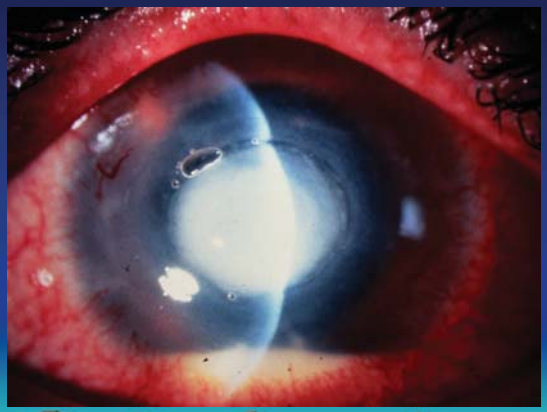
BACTERIAL ULCER/KERATITIS

- BIG THREE ORGANISMS:
  - S. AUREUS
  - S. PNEUMONIAE AND OTHER STREPTOCOCCI
  - PSEUDOMONAS

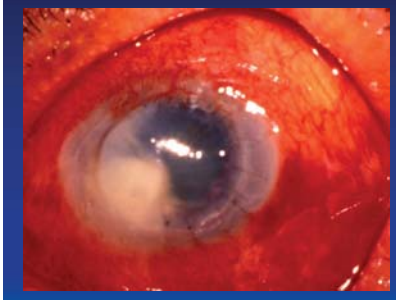
CLINICAL FEATURES

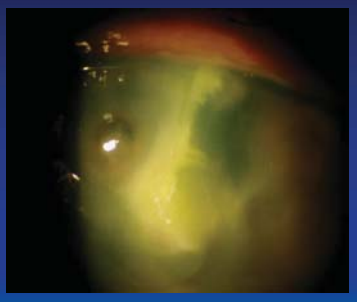
- GRAM POSITIVE:
  - S. AUREUS – LOCALIZED
  - STREP – DIFFUSE, RAPID PROGRESSION
- GRAM NEGATIVE:
  - P. AERUGINOSA: DIFFUSE, RAPID PROGRESSION

S. AUREUS KERATITIS

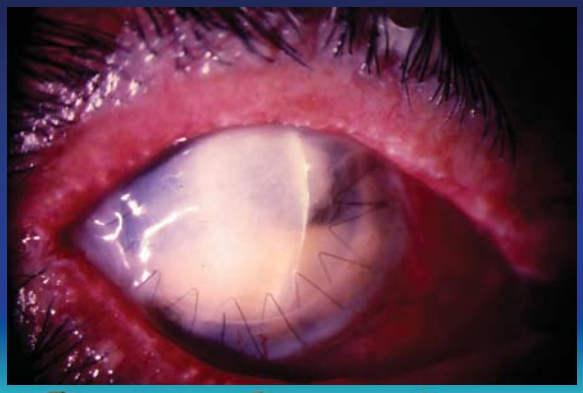


S. PNEUMONIA





P. AERUGINOSA



SPECIAL FEATURES

- RING ABSCESS:
  - P. AERUGINOSA
  - STREP
  - B. CEREUS / PROTEUS
- CRYSTALLINE KERATITIS
  - USUALLY STREP
  - RARELY FUNGAL

PATHOGENESIS

- JOHN HENLE (1840) SAID, “A HEALTHY BODY IS NOT A PROPER SOIL FOR INFECTIVE MATERIAL AND PRE-EXISTING CHANGES ARE REQUIRED TO PERMIT IT’S GROWTH AND PROLIFERATION”

PATHOGENESIS

- TRAUMA – ALLOWS INVASION OF BACTERIA FROM THE EYELID MARGINS
- IMMUNOSUPPRESSION
- EYELID GLOBE MALPOSITION, MALFUNCTION
- NLD OBSTRUCTION – OFTEN S. PNEUMONIA
- OCULAR SURFACE DISEASE (OSD)
- OLDER PATIENTS: TRICHIASIS, BLEPHARITIS

PREDISPOSITIONS

- TOPICAL STEROIDS → PNEUMOCOCCUS, FUNGUS, HSV
- ALCHOLISM → MORAXELLA, STREP SP.
- DIABETES → S. AUREUS
- CONTACT LENSES

NATURAL HISTORY

- PROGRESSIVE INFILTRATION
- THINNING / DESCEMETOCELE
- PERFORATION OR VASCULARIZATION
- SECONDARY GLAUCOMA
- ENDOPHTHALMITIS (1%)

CORNEAL ULCER WORK-UP

- KEEP CONTACT LENS, CASE AND SOLUTIONS FOR CULTURE AND CYTOLOGY

PATCHING

- PATCHING OF CORNEAL ABRASIONS IN C.L. WEARERS IS CONTRAINDICATED BECAUSE SOME ARE EARLY ULCERS

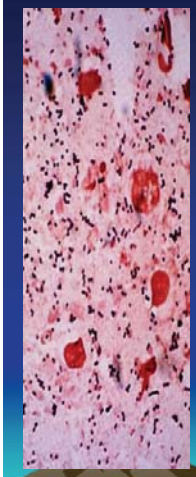
VIRULENT ORGANISMS

FEW ORGANISMS CAN PENETRATE AN INTACT EPITHELIUM:

- N. GONORRHEA
- C. DIPHTHERIA /LISTERIA /H. AEGYPTUS
- SOME FORMS OF PSEUDOMONAS

CORNEAL ULCER EVALUATION

- NOTE EXTENT OF CELLULAR RESPONSE
  - TEAR FILM
  - CORNEA
  - ANTERIOR CHAMBER
- STAIN WITH FLUORESCEIN
- MEASURE EPITH. DEFECT
- MEASURE INFILTRATE/ULCER SIZE

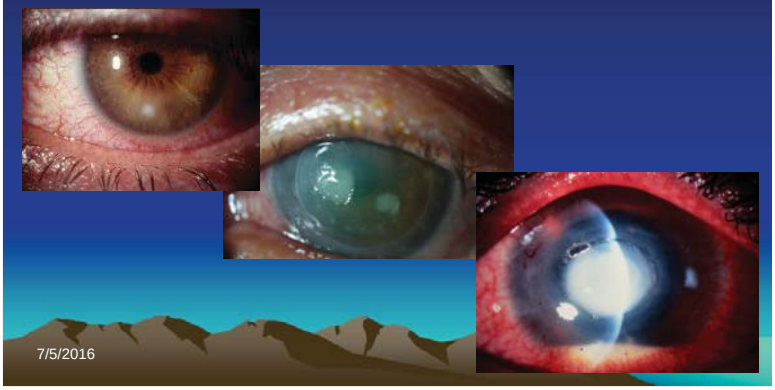


CORNEAL ULCER WORK-UP

- GRAM STAIN +/- GIEMSA STAIN
- CULTURE: BLOOD, CHOCOLATE AND SABRAUD'S AGARS (NOT NECESSARY FOR SMALL ULCERS)
- THIOGYCOLATE BROTH (ANAEROBES)
- LÖWENSTEIN-JENSEN MEDIUM (MYCOBACTERIUM)

CORNEAL ULCER MANAGEMENT

LESSOR CHALLENGE TO GREATER CHALLENGE



CULTURE RESULTS

- NO GROWTH – 44%
  USUALLY DUE TO PRIOR ABX
- MULTIPLE ORGANISMS – 6 TO 32%; WORSE PROGNOSIS

INDIGENOUS BACTERIA

- S. EPIDERMITIS, CORYNEBACTERIUM AND P. ACNES
  - RARELY ARE PRIMARY PATHOGENS
  - PARTICIPATE IN POLYMICROBIAL INFECTIONS

CULTURE RESULTS

7131 W GRANDRIDGE BLVD
KENNEWICK, WA 99336
(509) 736-0100

DOB: 10/15/1973 AGE: 33Y SEX: M
LOC: PROC

INTERIM REPORT

TEST NAME	RESULT	REF RANGE	UNITS	LAB LOC

T4251 COLL: 06/11/2007 18:45 REC: 06/12/2007 14:55 PHYS: URNESS,JEFFREY
Req# : PCLI12.F

NOT COLLECTED BY TCL

SUSCEPTIBILITY (CONTINUED)
1+ STAPHYLOCOCCUS HAEMOLYTICUS (1)

ORGANISM	MIC	(1)
METHOD		(1)
AMOX/CLAVULANIC ACID	RESISTANT	(1)
AMPICILLIN/SULBACTAM	RESISTANT	(1)
AZITHROMYCIN	SUSCEPTIBLE	(1)
CEFAZOLIN	RESISTANT	(1)
CEFOTAXIME	RESISTANT	(1)
CEFTRIAXONE	RESISTANT	(1)
CEFUROXIME	RESISTANT	(1)
CLARITHROMYCIN	SUSCEPTIBLE	(1)
CLINDAMYCIN	SUSCEPTIBLE	(1)
ERYTHROMYCIN	SUSCEPTIBLE	(1)
GENTAMICIN	SUSCEPTIBLE	(1)
OXACILLIN	RESISTANT	(1)
PENICILLIN G	RESISTANT	(1)
TETRACYCLINE	RESISTANT	(1)
VANCOMYCIN	SUSCEPTIBLE	(1)
IMIPENEM	RESISTANT	(1)
LEVOFLOXACIN	SUSCEPTIBLE	

(1) = Testing performed at TCL/7131 W Grandridge Blvd/Kennewick, WA 99336

WHAT THIS MEANS IS…

- THE ANTIBIOTIC SENSITIVITIES YOU GET FROM THE LAB MAY NOT ALWAYS APPLY TO THE CORNEA
- THE CORNEA IS A SPECIAL TISSUE

TREATMENT PRINCIPLES

- OUT PATIENT TREATMENT FOR NEARLY ALL ULCERS
- HOSPITAL ADMISSION – PATIENTS WHO CANNOT ADMINISTER FREQUENT DROPS
- INTENSIVE INITIAL TREATMENT WITH TOPICAL MEDICATIONS – Q 5 MIN IN OFFICE X 30 MINUTES, THEN Q 15” TO 30” x 6 – 8 HOURS, THEN Q 30” 24 - 48 HOURS.
- NO SUBCONJ. INJECTIONS
- ATROPINE 1% BID

ORAL / IV ANTIBIOTICS

- ORAL AND IV ANTIBIOTICS PENETRATE THE CORNEA POORLY
  - Doxycycline may be beneficial for wound repair effects and tear gland/lid margin modification
- USE FOR SCLERAL EXTENSION OR ENDOPHTHALMITIS

RESEARCH OF ABX EFFICACY
RABBIT MODEL: INFECTIOUS KERATITIS

- EXP. S. AUREUS KERATITIS RESPONDED BEST TO TOBRAMYCIN AND CIPRO
- VANCOMYCIN WAS LESS EFFECTIVE
- WELL ESTABLISHED INFECTIONS RESPONDED POORLY TO ALL ANTIBIOTICS

RESEARCH OF ABX EFFICACY
RABBIT MODEL: INFECTIOUS KERATITIS

- GENTAMICIN IS VERY EFFECTIVE FOR S. PNEUMONIA KERATITIS
- LITERATURE: FOR STREP, GENTAMICIN IS BETTER THAN TOBRAMYCIN

CONCLUSION

A TOPICAL FLUOROQUINOLONE +/- FORTIFIED GENTAMICIN IS THE BEST INITIAL TREATMENT FOR BACTERIAL KERATITIS

FORTIFIED GENTATMICIN PREP

- GENTAMICIN
  - 2 CC OF IV GENTAMICIN (40 MG/ML)
  - 5 CC BOTTLE OF GENTAMICIN EYEDROPS (3 MG/ML).
  - FINAL CONC = 13.6 MG/ML

STEROIDS FOR CORNEAL ULCER TRIAL (SCUT)

- MULTICENTER
- DOUBLE MASKED
- PLACEBO / CONTROLLED
- CLINICAL TRIAL
  - ARAVIND EYE HOSPITALS
  - DARTMOUTH-HITCHCOCK MEDICAL CENTER
  - UC SAN FRANCISCO
    - 500 patients enrolled

FOURTH GENERATION FLUORQUINILONES

- GATIFLOXACIN (ZYMAR)
  - EXPANDED GRAM + EFFICACY
- MOXIFLOXACIN (VIGAMOX)
  - EXPANDED GRAM + EFFICACY
- BESIFLOXIN (BESIVANCE)
  - EXPANDED GRAM + EFFICACY
    - MRSA & MRSE
  - SUSPENSION INCREASES CONTACT TIME, MAY DECREASE PENETRATION

STEROIDS FOR CORNEAL ULCER TRIAL (SCUT)

- PRIMARY OUTCOMES
  - BEST SPECTACLE CORRECTED VA (BSCVA) @ 3M
- SECONDARY OUTCOMES
  - BSCVA @ 3W & 12W
  - RIGID CL BVA @ 3M
  - PERFORATIONS
  - INFILTRATE/SCAR SIZE
    - CLINICAL
    - PHOTOGRAPHIC
  - RE-EPITHELIALIZATION TIME

STEROIDS FOR CORNEAL ULCER TRIAL (SCUT)

- INTERVENTION
  - 0.5% MOXIFLOXACIN
    - Q1h WHILE AWAKE X 48h THEN REDUCED
  - 1.0% PREDNISOLONE PHOSPHATE VS PLACIBO
    - INITIATED @ 48h
      - QID X 1 WEEK
      - BID X 1 WEEK
      - QD X 1 WEEK

STEROIDS FOR CORNEAL ULCER TRIAL (SCUT)

- SUMMARY: NO DIFFERENCE IN SAFETY OR EFFICACY
- SOME SUGGESTION THAT IN SEVERE ULCERS THERE MAY BE SOME BENEFIT
  - MORE STUDIES NEEDED

CORNEAL COLLAGEN CROSSLINKING

MODIFICATION OF TX

- MEASURE SIZE OF EPITH. DEFECT / INFILTRATE DAILY
- ULCER SHOULD BE LESS ACTIVE AFTER 24-48 HOURS
- CHANGE ANTIBIOTICS IF THE ORGANISM IS RESISTANT TO YOUR ANTIBIOTICS AND THE KERATITIS IS NOT RESPONDING

MODIFICATION OF TX

- IMPLICATION OF SCUTs (steroids for corneal ulcers trial)
  - STEROIDS WERE “SAFE” FOR CONFIRMED BACTERIAL KERATITIS
  - STEROID USE DID NOT IMPROVE TRIAL OUTCOMES

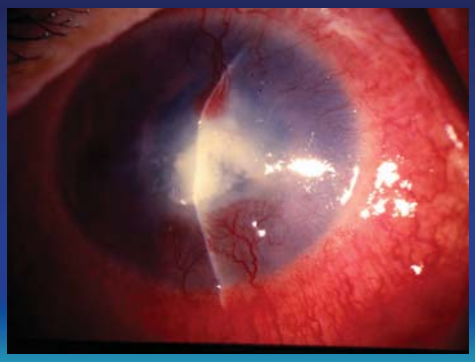
NO RESPONSE TO TX

- STOP ANTIBIOTICS FOR 8 TO 24 HOURS
- SCRAPE FOR STAINING AND CULTURE
- ? FUNGAL KERATITIS
- CORNEAL BIOPSY IF FUNGAL OR ACANTHAMOEBA POSSIBLE
- CONFOCAL SCAN, IF AVAILABLE

MELTING

- PSEUDOMONAS, STREP AND MORAXELLA TEND TO PERFORATE IN SPITE OF ADEQUATE TREATMENT – DUE TO PROTEOLYTIC BACTERIAL ENZMYMES

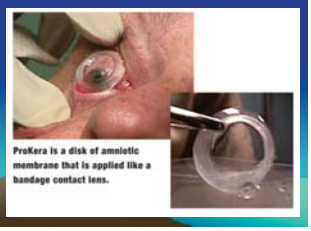
DESCEMETOCELE



WHAT CAN BE DONE?

TREATMENTS:

- GLUE C OR S BANDAGE LENS
- AMNIOTIC MEMBRANE
- CONJUNCTIVAL FLAP
- TARSORRHAPHY
- PATCH GRAFT
  OR FULL PKP



CONCLUSION

- TREATMENT OF INFECTIOUS KERATITIS:
  - AS A RULE, BEGIN BY TREATING ALL CORNEAL ULCERS AS IF THEY WERE BACTERIAL USING FLUOROQUINILONE + FORTIFIED GENTAMICIN OR FORTIFIED VANCOMYCIN

WHEN TO REFER?

- LARGE ULCERS
- ULCERS THREATENING VISUAL AXIS
- AGGRESSIVE ULCERS OR ULCERS THAT DON'T RESPOND IN 48 HOURS

CONSIDER REFERRAL TO CORNEAL SERVICE

THANKS FOR COMING

Pediatric Case Reports: The Good, Bad, and the Ugly

Dr. Kathleen Elliott
drelliott1111@yahoo.com

Description:
What is really important in pediatric evaluations? What are the warning signs of an eye gone bad? These and many other questions will be answered when this course arms you with the ammo you need to get up to speed on recognizing pediatric eye problems. You will explore case reports that include infantile strabismus, optic nerve disorders, systemic and ocular neurological disorders, extraocular muscle disorders, and eyelid and trauma cases. Additionally, advice on handling abuse cases, and the ocular pharmacological side effects of systemic medications will be addressed.

Objectives:
1. To recognize common pediatric abnormalities and understand treatment options for those conditions.
2. To review pediatric case reports pertinent to caring for the pediatric patient.
3. To know and recognize systemic and ocular manifestations of neurological and pathological disease processes in the pediatric population.

Outline:

I. INFANTILE ESOTROPIA

A. DEFINITION: (aapos.org): A sensory and /or motor dysfunction causing one or both eyes to turn inward. It begins at birth or in the first year of life. There is an increased risk for the development of amblyopia with this condition.

B. RISK FACTORS:

- prematurity,
- hydrocephalus,
- seizure disorders,
- neurodevelopmental delay
- family history of strabismus

C. TREATMENT OPTIONS: Most viable options include

- Surgery is performed after any amblyopia is treated and the eso is stable. Surgery performed prior to 2yo has been found to give better long term results, with a reoperation rate as low as 11% to as high as 69%.

- Botulinum toxin in select cases.

II. EXTRAOCULAR MUSCLE DISORDERS:

A. DUANES SYNDROME: congenital mis-wiring of horizontal movement muscles.

- type 1: Lateral Rectus mis-wiring and the patient cannot AB-duct the eye. look also for lid fissure narrowing. typically female pt, left eye most common in Duanes type 1 cases.
- Duane's type II: cannot AD-duct eye and
- Type III: can neither AB nor AD duct the eye.

B. BROWNS SYNDROME: Known as Superior Oblique Tendon Sheath Syndrome

- The S.O. muscle/tendon does not move freely
- Looking up & in for the affected eye is difficult
- In horizontal gaze, looking toward affected eye, one eye appears higher when looking up.
- Often the higher eye is mistakenly presumed to be abnormal, but the lower eye is the affected one.(aapos.org)

C. Marcus Gunn Jaw -Wink:a.k.a. Trigemino-oculomotor Synkinesis(wikipedia.org)

- Nursing infants will have a rhythmic upward jerking of upper eyelid.
- Commonly occurs during sucking, chewing, or conjugate eye movements
- Presents in 5% of neonates with congenital ptosis
- Associated with amblyopia & strabismus(55%occurance)

III. CASE REPORTS

A. OPTIC NERVE DRUSEN: A 9 year old female presents with headaches x 6 weeks, no ataxia, no nausea/vomiting, no diplopia. VA 20/20 unilaterally & bilaterally. Visual field normal (FFC).

+1.00 OU cycloplegic refraction. Upon dilation, 78d lens reveals 3+elevation of both optic nerves.

1. Work up should include?
2. What if ultrasound indicates swelling vs. drusen?
3. MRI first or Lumbar Puncture first?

B.RETINOBLASTOMA: A 6 week old male presents with a unilateral white reflex that the pediatrician found when checking for red retinal reflex.

1. What ocular (retinal) sign and symptoms would you expect to view with the BIO?
2. What would your work-up include? Referral Guidelines?
3. What would be included in your differential diagnosis?

IV. CONCLUSIONS/QUESTIONS/ANSWERS/FINAL THOUGHTS

SETTING UP A DRY EYE PRACTICE

VICTORIA, BC

Amber Gaume Giannoni, OD, FAAO, Diplomate (ABO)
Director, Dry Eye Center (UHCO)
Email: agaume@optometry.uh.edu

DISCLOSURES

- Advisory Boards:
  - Vistakon
  - Allergan
  - Alcon
  - OSSO Board
  - Advanced Ocular Care Editorial Board
- Speaker's Bureau:
  - Alcon

I have no financial or proprietary interests relative to this presentation

Is It Worth It?

....Worth it to your patients?

- Dry eye disease is <u>common</u>
- Risk factors are increasing:
  - Aging population
  - Increased meds
  - DM/autoimmune disease
- Quality of life (QOL):
  - Increase risk anxiety/depression
  - Mild DE QOL = psoriasis
  - Severe DE QOL = disabling hip fracture
  - **Would give up a year of life**


dry eye dx and tx

The Impact of Dry Eye on Quality of Life

….Worth it to you?

TABLE 2 Economic Potential of Dry Eye in the Average Optometric Practice

Number of Americans who have dry eye	78,500,000
Median patient volume in an optometric practice per year	3,100
Overall incidence of combined dry eye	25%
Dry eye patients in an optometric practice per year	775
Average reimbursement for dry eye-related office visit	$73
Typical number of office visits for a dry eye patient per year (non-punctal occlusion)	3
Potential revenue from dry eye office visits per year (non-punctal occlusion)	$164,633.25
Typical revenue from a Medicare punctal occlusion patient	$756.88
Typical revenue from a non-Medicare punctal occlusion patient	$1,336.60
Percentage of patients undergoing punctal occlusion	3%
Potential punctal occlusion revenue from Medicare patients per year (assuming half of the practice's volume is Medicare patients)	$8,798.73
Potential punctal occlusion revenue from non-Medicare patients (assuming the other half of the practice's volume is non-Medicare patients)	$15,537.96
Potential revenue due to dry eye per year	$188,969.94
Lifetime economic potential of diagnosing and treating dry eye	$8,503,647

Newman C, Rumpakis J 2014

Percentage of eye care practitioners that screen for dry eye disease

A. 100%
B. 75%
C. 50%
D. 25%

18%

Percentage of ***diagnosed*** patients that are put on dry eye treatment?

A. 100%
B. 75%
C. 50%
D. 25%

<50%

- "Don't have time"
- "No good screening method"
- "Diagnosis and treatment guidelines are too complicated"
- "Treatments don't work so why bother?"

- Possible to provide effective and efficient management for DED
- Have most of what you need to diagnose and treat dry eye already
- May need access to devices and technology specific to DED
- Treatment WORKS if you start early enough

If **WE** aren't actively looking for and treating dry eye disease **who will**?

Meanwhile, our patients will continue to progress…..

Setting up a Dry Eye Practice

STEP 1: Educate yourself

STEP 2: Educate/utilize/empower staff

STEP 3: Prepare patient education materials

STEP 4: Implement your vision

STEP 1: EDUCATE YOURSELF

- **Know the risk factors**
  - Who do you screen?
  - What are you screening for?
  - Who should you treat aggressively?
- **Understand differences between sub-types**
  - Targeted treatment plans

STEP 1: EDUCATE YOURSELF

- **CAN'T rely on symptoms**
  - Patients often don't tell
  - Symptoms often don't match disease state
- **Diagnostic testing order matters!**
  - One test will affect the next
  - Generally least invasive to most invasive

One Suggested Testing Order*

(least to most invasive):

1. Dry eye questionnaire and targeted history
2. Osmolarity and/or inflammatory markers
3. NITBUT (keratometer, keratograph or topographer)
4. Tear volume (i.e. phenol red thread)
5. SLE including:
   - Tear prism/quality/debris
   - Vital dye staining
   - Lid and MG evaluation/diagnostic expression
6. Meibography/lid eversion

*Based on DEWS 2007

STEP 1: EDUCATE YOURSELF

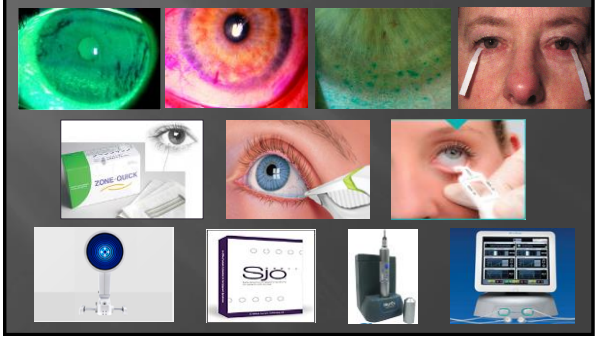
- **Know disease staging**
  - Initiate appropriate treatment level
- **Research targeted treatment plans**
  - Shoot-in-the-dark approaches don't work

RESOURCES

- *Delphi Dry Eye Panel 2006
- *International Dry Eye Workshop 2007 (IOVS)
- *International Workshop on MGD 2011 (IOVS)
- *Call a friend/take a field trip!
- CE lectures (AAO)
- *Social Media (OD's for OSD – Facebook)
- *Newsletters (Ocular Surface News)
- Ocular Surface Societies:
  - *Tear Film and Ocular Surface Society (TFOS)
  - Ocular Surface Society of Optometry (OSSO)

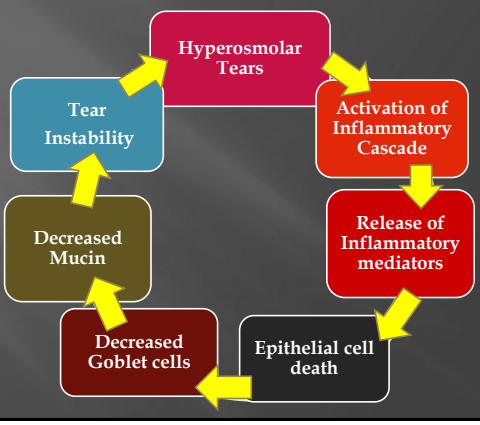
*FREE!

Diagnostic and Therapeutic Equipment



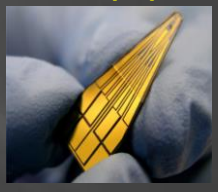
"...a multi-factorial disease of the tears and ocular surface that results in symptoms of discomfort, visual disturbance and tear film instability with potential damage to the ocular surface. It is accompanied by **increased osmolarity of the tear film** and inflammation of the ocular surface."

-2007 Report of the International Dry Eye Workshop (DEWS)



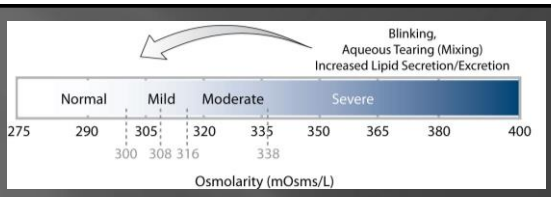
"Lab on a microchip"

TEARLAB™ Osmolarity System



Measures conductivity of 50 nL tear sample using gold electrodes and converts to osmolarity

Michael Lemp MD FACS
David C Eldridge OD FAAO



Prevalence of DED Using Hyperosmolarity (n=8800)

- Normal inter-eye difference: **7 ± 6 mOsm/L**
- Dry eye inter-eye difference: 1**7 ± 15 mOsm/L**

Tells you <u>YES</u> or <u>NO</u>, not WHY or HOW

Lemp MA et al., 2011

Accuracy:

- 88% specificity, 75% sensitivity in mild-moderate DE
- 95% sensitivity in severe disease
  - Decrease in compensatory mechanism as disease progresses

Foulks GN et. al. 2009

CLINICAL APPLICATION

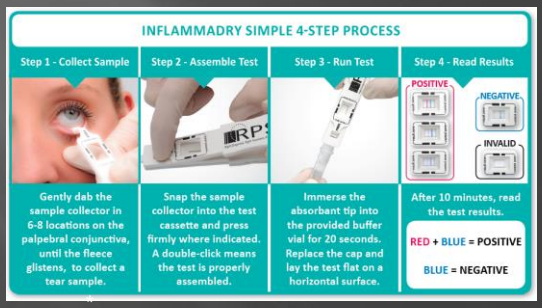
- Great screening tool for general population:
  - Early intervention
  - Properly generate medical dry eye return visits
- Provides objective information:
  - Helps stage DED severity when signs/symptoms don't match
  - Monitor therapeutic efficacy

"...a multi-factorial disease of the tears and ocular surface that results in symptoms of discomfort, visual disturbance and tear film instability with potential damage to the ocular surface. It is accompanied by increased osmolarity of the tear film and

inflammation of the ocular surface."

-2007 Report of the International Dry Eye Workshop (DEWS)

INFLAMMADRY (RPS)



Untreated inflammation can lead to:

- Decreased lacrimal gland function
- MGD
- Epithelial in-growth or LASIK flap slippage
- Inaccurate pre-op tests
- Difficult healing post-surgery

Asymptomatic, mild dry eye can becomes severe, symptomatic, chronic dry eye

Fournie PR et al 2010

CLINICAL APPLICATION

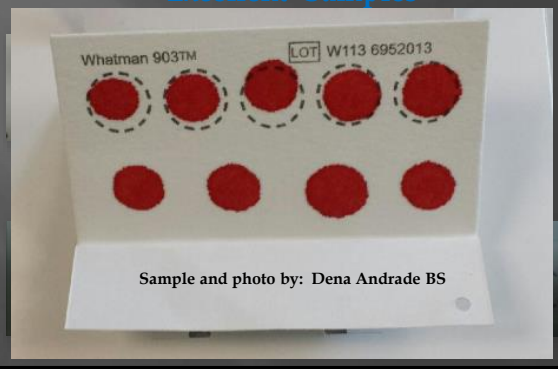
- Predict which patients will respond to anti-inflammatory therapy
- Monitor therapeutic intervention as it relates to MMP-9
- Prior to punctal occlusion

*Remember, MMP-9 is only one of many inflammatory markers and it is **non-specific** for dry eye disease

Sjö ™ Laboratory Test (B&L)

Includes classic SS biomarkers plus 3 new proprietary markers

Excellent Samples



Sample and photo by: Dena Andrade BS

A reminder….

Sjogren Syndrome:

- One of the most common autoimmune diseases
  - 1% of the population
  - Only ¼ diagnosed
  - Average time to diagnosis is 5-7 years
- Can affect every organ system
- Higher risk of lymphoma
- Optometry is in a unique position to be the first diagnose this disease!

Blood work in Sjogren's Syndrome:

- ANA (+)…….70% (non-specific)
- RF(+) ……60-70% (non-specific)
- ESR ……..80% show elevation (non-specific)
- Anti-Ro/SS-A (+)…….60-70% ("specific")
- Anti-La/SS-B (+)…….40% ("specific")
  - Not often positive in early stages
  - 25-35% of SS patients are negative for SS-A and SS-B

Sjo Organ-Specific Biomarkers:

SP-1 – Salivary Protein 1:
- High expression in lacrimal and submandibular glands

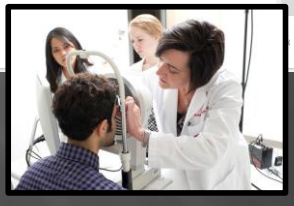
CA6 – Carbonic Anhydrase 6:
- High expression in submandibular and parotid glands

PSP – Parotid Secretory Protein:
- High expression in the acinar cells of the salivary glands

Current Screening	New SS Panel
• Combined sensitivity & specificity is 40-60%	• Combined sensitivity & specificity is 82.5% - 87% • Cumulative specificity is 92.2%
• None of the "classic" serology tests diagnose early cases	• Identifies ~50% of early cases (Ro and La Negative)
• Miss approximately 25-35%	• Should pick up additional cases

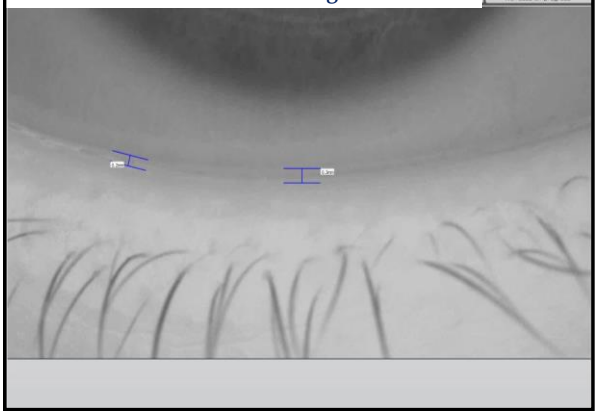
1. Tincani A, et al. Novel aspects of Sjögren's Syndrome in 2012. BMC Med Apr 4 2013;11:93. doi: 10.1186/1741-7015-11-93. 2. Shen L, et al. Novel autoantibodies in Sjogren's Syndrome. Clin Immunol 2012;145:251-255. 3. Huang Y, et al. The immune factors involved in the pathogenesis, diagnosis, and treatment of Sjogren's Syndrome. Clin Dev Immunol 2013; Article ID 160491. doi:10.1155/2013/160491. 4. Ramos-Casals M, Brito-Zeron P, Siso-Almirall A, Bosch X. Primary Sjogren's Syndrome. BMJ 2012;344:e3821

Oculus Keratograph 5M

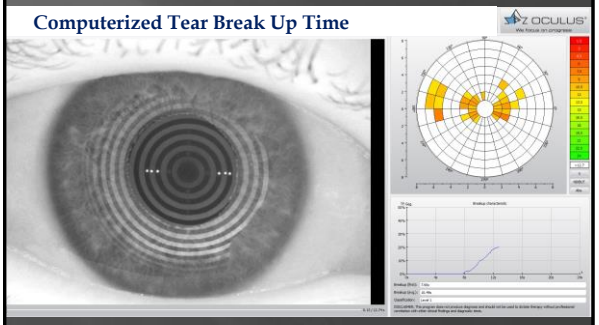


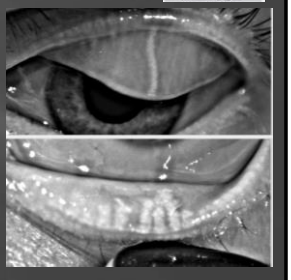
- Topography
- Tear Meniscus Height
- Redness grading
- Non-Invasive break-up
- Infra-red meibography
- Tear lipid quality
- HD photos and videos

Tear Meniscus Height



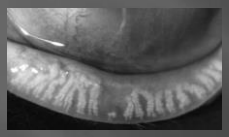
Computerized Tear Break Up Time

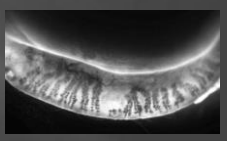




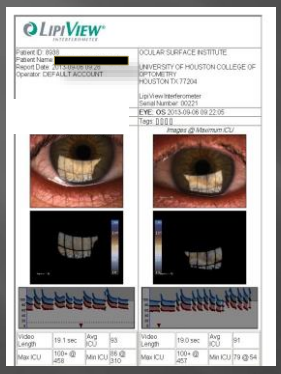
Infra-red meibography

LipiView (TearScience)





[Photos courtesy of TearScience]



- Analyzes 1 billion data points
- Measures:
  - Absolute lipid thickness
  - Tear spreading
  - Partial blinks

Evaluating Specialty Equipment

GOALS:

- Simple and run by trained technicians (if possible)
- Highly sensitive
- Highly selective/specific
- Repeatable
- Useful
- Cost/Profit

DRY EYE TESTS

Test	Positive Agreement (Sensitivity)	Negative Agreement (Specificity)
InflammaDry[1-2]	81-85%	94-98%
Schirmer Tear Test[3]	42%	76%
Tear Break Up Time (T-BUT)[3]	92%	17%
Corneal Staining[3]	63%	89%
TearLab Osmolarity System[4-5]	64-90%	71-92%
Questionnaire[3]	89%	72%

RPS Clinical Study, Sambursky R et. al. JAMA Ophthalmol 2013

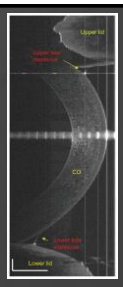
RPS InflammaDry positive agreement and negative agreement was compared to clinical truth in RPS clinical study: protocol #12-0615. [2] Sambursky R, Davitt WF 3rd, Latkany R, et al. Sensitivity and specificity of a point-of-care matrix metalloproteinase 9 immunoassay for diagnosing inflammation related to dry eye. JAMA Ophthalmol. 2013 Jan;131(1):24-8. [3] Versura P, Frigato M, Cellini M, et al. Diagnostic performance of tear function tests in Sjogren's syndrome patients. Eye (Lond). 2007 Feb;21(2):229-37. [4] FDA Section 510(k) number k083184 for TearLab™ Osmolarity System; May 5, 2009. [5] Lemp MA, Bron AJ, Baudouin C, et al. Tear osmolarity in the diagnosis and management of dry eye disease. Am J

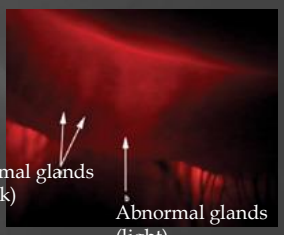
There's a lot we can do with what we already have in the office though too….

Questionnaires:

- Simple
- Screen/follow therapeutic progress
- Staff or self-administered ☺
- Paper or electronic:
  - Ocular Surface Disease Index (OSDI)
  - Standard Patient Evaluation of Eye Dryness (SPEED)
  - Dry Eye Questionnaire (TearLab)
  - Dry Eye Questionnaire (McMonnies & Ho)
  - Industry tools

- **Tear volume:**
  - Tear prism
  - Phenol red thread or Schirmer test
  - OCT
- **Corneal and conjunctival staining**
  - NaFL/cobalt filter
  - Lissamine green/white light
  - Fluramine (combo)
- **TBUT**
  - NaFl
  - Keratometer
  - Topographer





Paugh J. Contact Lens Spectrum 2005

What About Therapeutic Equipment??

"Lid hygiene is regarded as the mainstay in the clinical treatment of MGD. It usually consists of two components: application of heat and massage of the eyelids."

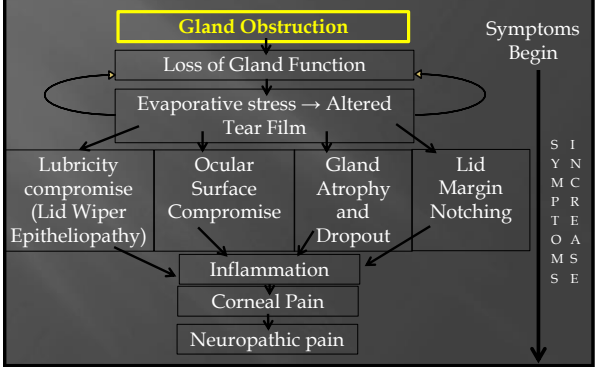
Geerling G, Tauber J, Baudouin C, Goto E, Matsumoto Y, O'Brien T, Rolando M, Tsubota K, Nichols KK. The international workshop on meibomian gland dysfunction: Report of the subcommittee on management and treatment of meibomian gland dysfunction. Invest Ophthalmol Vis Sci. 2011 Mar 30;52(4):2050-64

- Melting point of MG secretions:
  - Normals @ 32° C (89° F)
  - MGD @ 35° C (95° F)
- Hot compresses 15 min followed by lid massage qd-qid to:
  - Improve MG secretion quality
  - Improve lipid layer
- Washcloths don't work well:
  - Not hot/long enough
  - Evaporation = cooling

Heat Masks

- Better results
- Spend money – more apt to do the therapy
- More "professional"
- Revenue

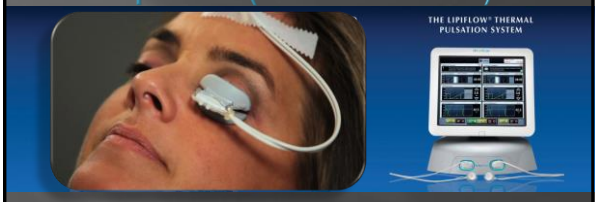
MGD PATHOPHYSIOLOGY



MGD Pathophysiology

- Meibomian gland atrophy begins with obstruction
- To properly treat MGD and prevent progression, obstructions need to be removed:
  - Home massage/pinch
  - In-office expression
    - Automated
    - Manual

Automated Expression Lipiflow (TearSciences)



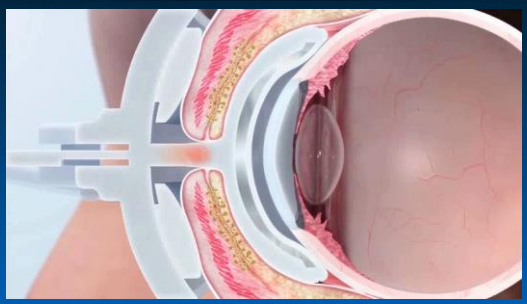
Cornea. 2012 Apr;31(4):396-404.

A new system, the LipiFlow, for the treatment of meibomian gland dysfunction.

Lane SS, DuBiner HB, Epstein RJ, Ernest PH, Greiner JV, Hardten DR, Holland EJ, Lemp MA, McDonald JE 2nd, Silbert DI, Blackie CA, Stevens CA, Bedi R.
Associated Eye Care, Stillwater, MN, USA.

CONCLUSION: The LipiFlow System was significantly more effective than iHeat WC. These results support its safety and effectiveness in the treatment of MGD and dry eye symptoms.

Applies heat and pressure at the same time, requires placement of a corneal shield
~12 minute treatment; FDA approved



TearScience®

Korb, DR, Blackie, CA. Meibomian gland therapeutic expression: quantifying the applied pressure and the limitation of resulting pain. *Eye Contact Lens.* 2011 Sep;37(5):298-301.

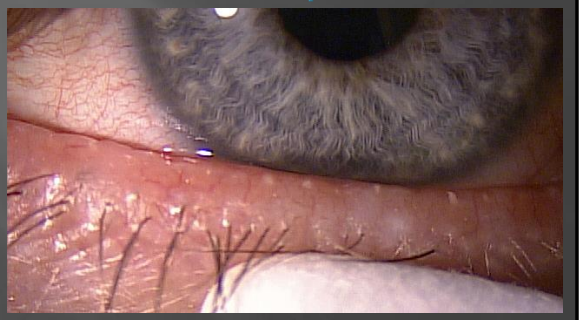
Lipiflow (TearScience):

- 76%: symptom improvement within 2 weeks
  - Versus 56% using warm compresses[1]
- Single treatment can last more than 12 months[2]
- May take several months and re-treatment for full benefit
- Re-treatment required for chronic sufferers

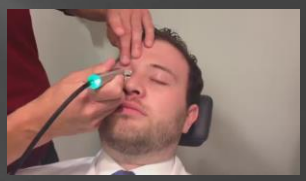
1.Stephen S. Lane et. al, Cornea 2012
2.Greiner JV et. al 2011

No Lipiflow?

Mechanical Therapy: In Office Expression



MiBoFlo (Pain Point Medical, Inc)



- Reduce biofilm
- Reduce bacterial load
- Clear scurf

I Don't Have a LipiFlow, BlephEx, MiboFlo, etc, etc, etc.

- Refer to ODs who do the procedure
- Consider joint ownership
- Manage the follow-up:
  - Many individuals who undergo these procedures become symptomatic again – need f/u care!
  - Become an expert in post-op management of these procedures

Unlike diagnostic testing, dry eye therapeutics are often out-of-pocket expenses

New technology can be costly and overwhelming BUT, can also:

- Improve detection strategies for earlier intervention
- Demonstrate improvement to encourage compliance
- Make dry eye care more successful and a lot more fun!

STEP 2: EDUCATE STAFF

- The AVERAGE OD is worth $5.35/min!
- Staff is the key to efficient and profitable management of eye disease!
  - Administer questionnaires – to who?
  - Conduct applicable diagnostic testing – on who?
  - Properly educate patients on recommendations and home care – how?

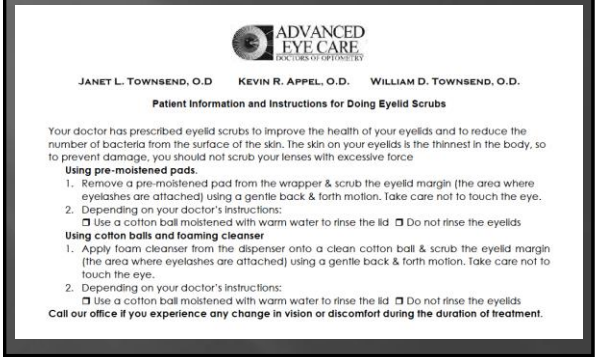
STEP 2: EDUCATE STAFF

- Hands-on training/point person/cross-over
- Lunch n' Learns
  - Conducted by practice owner or industry reps
- Experience treatment options
  - Bring excitement and personal experience

STEP 3: EDUCATE PATIENTS

- KEY to compliance!
- In-the-chair discussion with doctor
  - Photography/slit lamp videos
  - Cell phone!
- Staff-delivered education
  - Verbal; Handouts; ipad
- Directed education
  - Office website, web

Handouts Enhance Compliance



ADVANCED EYE CARE
DOCTORS OF OPTOMETRY

JANET L. TOWNSEND, O.D KEVIN R. APPEL, O.D. WILLIAM D. TOWNSEND, O.D.

Patient Information and Instructions for Doing Eyelid Scrubs

Your doctor has prescribed eyelid scrubs to improve the health of your eyelids and to reduce the number of bacteria from the surface of the skin. The skin on your eyelids is the thinnest in the body, so to prevent damage, you should not scrub your lenses with excessive force

Using pre-moistened pads.

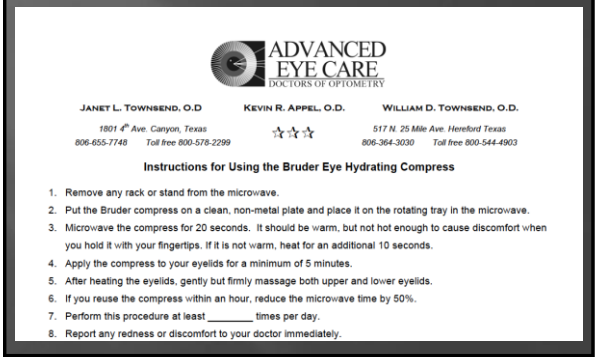
1. Remove a pre-moistened pad from the wrapper & scrub the eyelid margin (the area where eyelashes are attached) using a gentle back & forth motion. Take care not to touch the eye.
2. Depending on your doctor's instructions:
   ❒ Use a cotton ball moistened with warm water to rinse the lid ❒ Do not rinse the eyelids

Using cotton balls and foaming cleanser

1. Apply foam cleanser from the dispenser onto a clean cotton ball & scrub the eyelid margin (the area where eyelashes are attached) using a gentle back & forth motion. Take care not to touch the eye.
2. Depending on your doctor's instructions:
   ❒ Use a cotton ball moistened with warm water to rinse the lid ❒ Do not rinse the eyelids

Call our office if you experience any change in vision or discomfort during the duration of treatment.

Handouts Enhance Compliance



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JANET L. TOWNSEND, O.D KEVIN R. APPEL, O.D. WILLIAM D. TOWNSEND, O.D.

1801 4th Ave. Canyon, Texas 806-655-7748 Toll free 800-578-2299

517 N. 25 Mile Ave. Hereford Texas 806-364-3030 Toll free 800-544-4903

Instructions for Using the Bruder Eye Hydrating Compress

1. Remove any rack or stand from the microwave.
2. Put the Bruder compress on a clean, non-metal plate and place it on the rotating tray in the microwave.
3. Microwave the compress for 20 seconds. It should be warm, but not hot enough to cause discomfort when you hold it with your fingertips. If it is not warm, heat for an additional 10 seconds.
4. Apply the compress to your eyelids for a minimum of 5 minutes.
5. After heating the eyelids, gently but firmly massage both upper and lower eyelids.
6. If you reuse the compress within an hour, reduce the microwave time by 50%.
7. Perform this procedure at least _____ times per day.
8. Report any redness or discomfort to your doctor immediately.

STEP 4: IMPLEMENT !

- Determine scheduling:
  - Time block for initial work-up vs. follow-ups
  - Book alongside other patients or have dedicated day?
    - Establishes mind-set for staff/doctors
    - Patients “talk” in waiting room
- Advertise!
  - STAFF; Word-of-mouth
  - Office website
  - Rheumatology, PCP, endocrinology, other ODs, OMDs

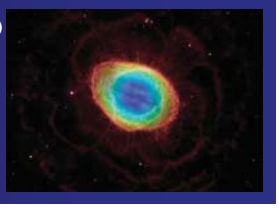
Conclusion

- Management of OSD can be rewarding !
- Use of ancillary personnel creates a “team spirit”
- Setting up a dry eye practice requires:
  - Education
  - Preparation
  - Investment
- GO FOR IT! It is well worth it!!

I will praise thee; for I am fearfully and wonderfully made!
Psalm 139: 14

Corneal Transplantation: Front To Back Side To Side

(COPE 40409PO)



James McNeill MD

James Guzek MD

Objectives

- Review pertinent anatomy & immunology
- Review diagnostic characteristics that impact surgical decisions
- Demonstrate surgical management
- Present post operative management

Background

- Corneal grafts represent the first successful solid tissue transplants in medicine
- They are the most common & successful tissue transplant techniques in medicine
- This doesn't mean management of these patients is simple or straightforward

Cornea Transplantation

- 5 keys to understanding grafting
  - The fate of transplanted nucleated cells
  - Endothelial function and decline
  - Immunologic nature of the cornea
  - Tissue repair and remodeling
  - Understanding how the graft type and indication for grafting effects outcomes

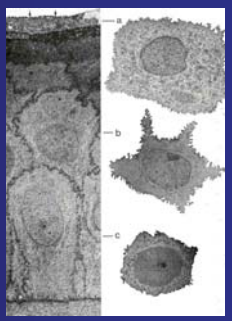
Corneal Anatomy & Physiology

- Tear Film (7-10 um)
  - Lipid (0.1 um)
  - Aqueous (7-10 um)
  - Mucin (0.02-0.05 um)

- Tear Film Dynamics
  - TBUT (>15s)
  - Schirmer/Phenol Thread (>10mm)

Corneal Anatomy & Physiology

- Epithelium (50um, 8%)
  - Histology/Morphology
  - Function
  - Reproduction
  - Migration
  - Remodeling



Corneal Anatomy & Physiology

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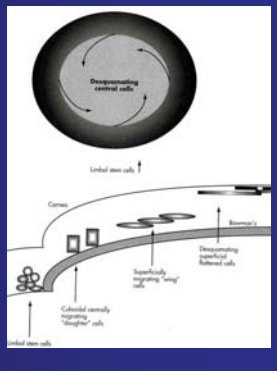
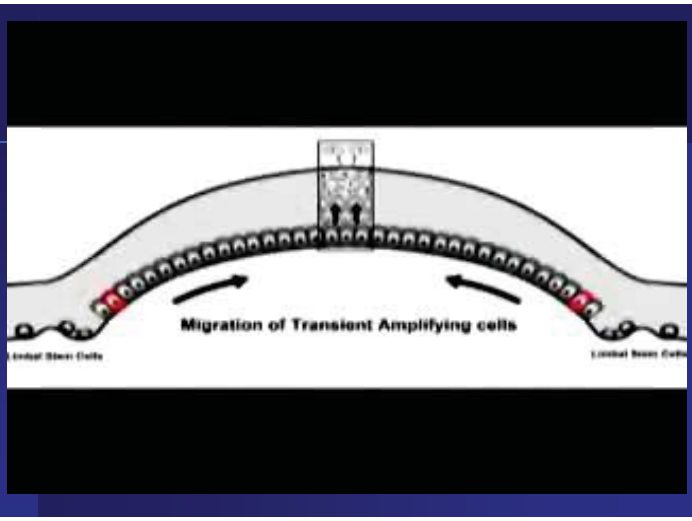
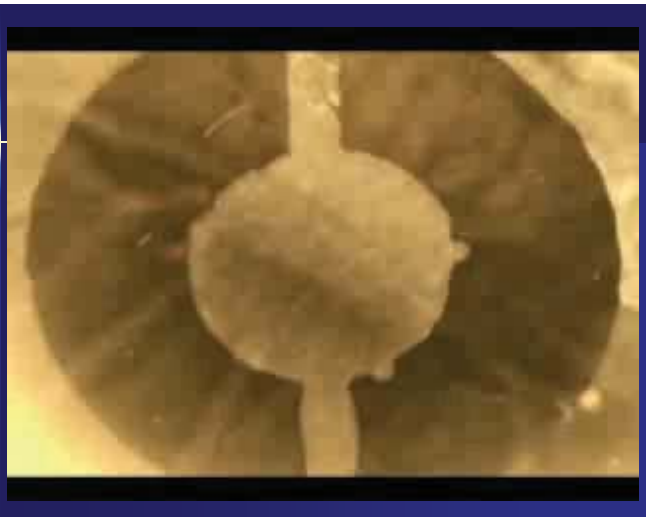
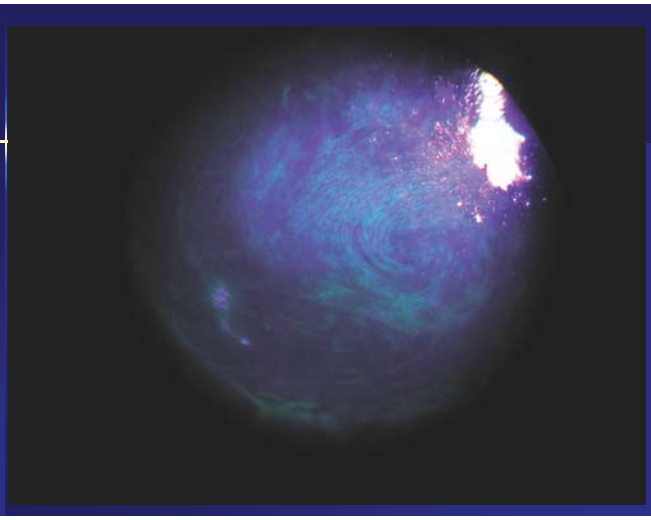


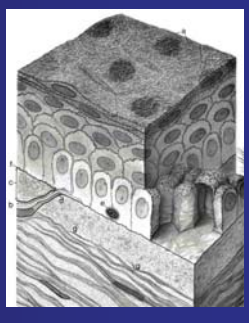






Corneal Anatomy & Physiology

- **Bowman's Layer (12um, 2%)**
  - Histology/Morphology
  - Repair/Remodeling
  - Function

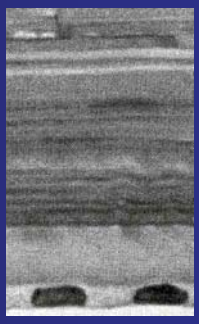


Corneal Anatomy & Physiology

- **Stroma** (500um, 90%)
  - Histology/Morphology
  - Repair/Remodeling
  - Function
  - Dua's layer

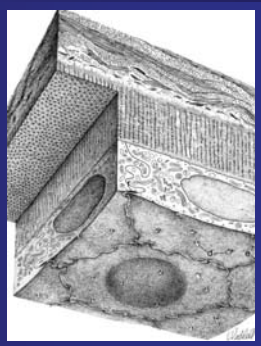
Corneal Anatomy & Physiology

- **Descemet's Layer** (7um, 1%)
  - Histology/Morphology
  - Remodeling/Repair
  - Function



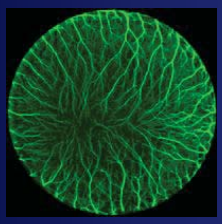
Corneal Anatomy & Physiology

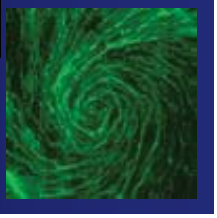
- **Endothelium** (5um, 1%)
  - Histology/Morphology
  - Reproduction
  - Repair
  - Function



Corneal Anatomy & Physiology

- Neurons
  - Histology
  - Reproduction
  - Function





Corneal Anatomy & Physiology

- Tear Film (7-10um)
- Epithelium (50um, 8%)
- Boman's Layer (12um, 2%)
- Stroma (500um, 90%)
- Descemet's Membrane (7um, 1%)
- Endothelium (5um, 1%)
- Neurons (50 trunks)

Corneal Immunology

- Considered immune privileged
  - Lack of both afferent (lymphatic) and efferent (vascular) arms of immune system
  - Lack of substantial load of native immune cells/APC
  - Weak expression of Major Histo Compatability (MHC) antigens
  - Beneficiary of the Anterior Chamber Associated Immune Deviation (ACAID)

Conditions Treated With Transplant

Post Cataract Surgery Edema	25.6%
Keratoconus & Pellucid Degenerations	22.8%
Fuchs' Dystrophy	14.4%
Repeat Corneal Transplant	13.3%
Other Deg' & Dystrophies	1.8%
Post-Refractive Surgery	6.0%
Microbial Changes	8.1%
Trauma	6.0%
Congenital Opacities	0.0%
Other	2.1%

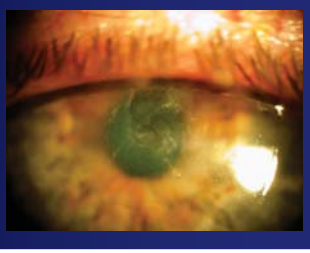
KPCLI

Guidelines For Pursuing Transplant

- Anatomic indications
  - Optical
  - Structural
  - Cosmetic
- Functional indications
  - Often most significant
- Clinical indications
  - Diseases and situations prompting transplant

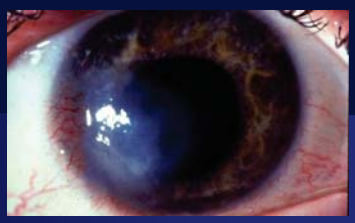
Prognostic Classification

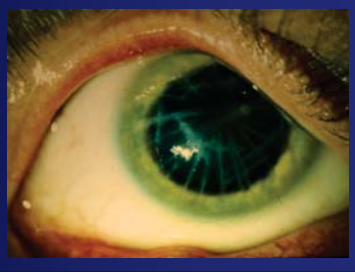
- Group 1: Excellent
  - 90% success
  - Avascular
  - Central thinning &/or clouding
    - Keratoconus
    - Inactive scarring
    - Central dystrophies



Prognostic Classification

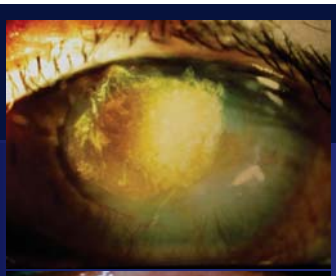
- Group 2: Very Good
  - 80% success
  - Lesions involving part or all of surgical surface
  - Mild to moderate vascularization 1 or 2 quadrants

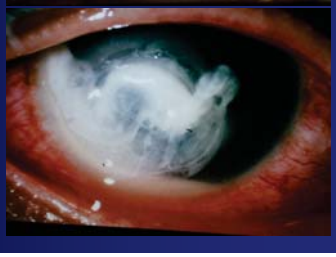




Prognostic Classification

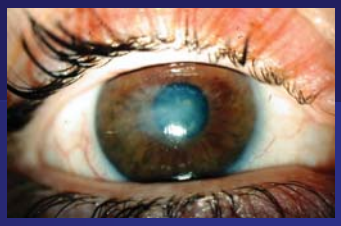
- Group 3: Fair
  - 50% to 80% success
  - Extremes of corneal thickness
  - Perforations
  - Peripheral descemetocele
  - Infection or inflammation
  - Mild chemical burn
  - Moderate sicca

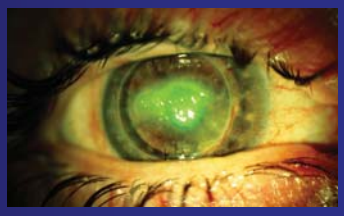




Prognostic Classification

- Group 4: Poor
  - < 50% success
  - Severe fibrovascular replacement
  - Conjunctival ischemia
  - Severe sicca
  - Severe chemical burns
  - Multiple graft failures
  - Neuroparalytic or neurotrophic disease
  - Mucous membrane disorders



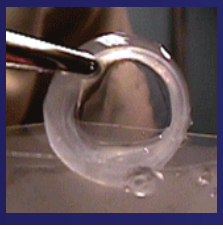


Corneal Prothesis

- Used for eyes with high risk for graft failure
- Usually monocular patient
- Need to have adequate ocular surface environment

Corneal Amniotic Graft

- Used for eyes with high risk for surface healing complications



Intra-stromal Avastin Injections

- Early use in "rescuing" vascularizing corneas
- May have preoperative prophylactic benefit

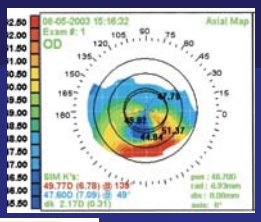
Intra-stromal Avastin Injections

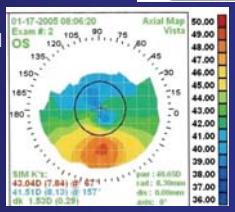
Ectatic Diseases

- Keratoconus
- Pellucid Degeneration
- Post Inflammatory
- Post Surgical
- Post Trauma

Keratoconus & Pellucid Degenerations

- Diagnostic features
  - Unstable refraction
  - Poor spectacle corrected vision
  - Characteristic irregular corneal contour
  - Characteristic corneal thinning
  - Iron deposition
  - Striae
  - Scarring





Keratoconus & Pellucid Degenerations

- Diagnostic features
  - Unstable refraction
  - Poor spectacle corrected vision
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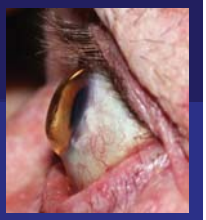

Keratoconus & Pellucid Degenerations

- Diagnostic features
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Keratoconus & Pellucid Degenerations

- Diagnostic features
  - Unstable refraction
  - Poor spectacle corrected vision
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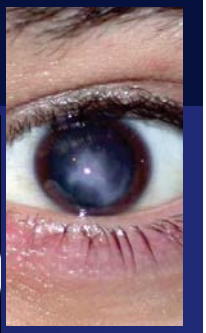
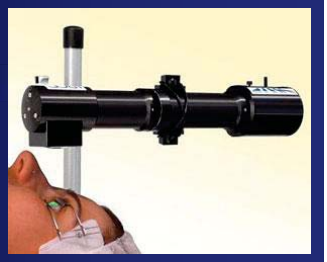
  - Iron deposts
  - Striae
  - Scarring



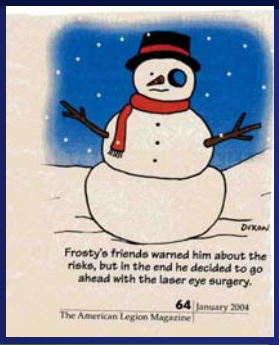
Keratoconus & Pellucid Degenerations

- Medical management
  - Corneal crosslinking
    - UV + Riboflavin produces "inter-molecular bonds"
    - Cornea becomes more rigid
  - Allergy tx and avoidance of eye rubbing
  - Contact lens tx



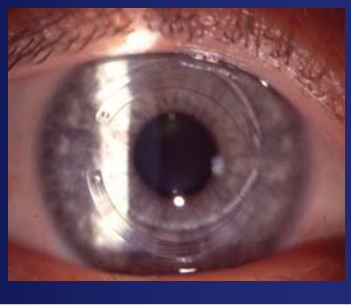
Keratoconus & Pellucid Degenerations

- Surgical management
  - NO corneal thinning procedures (PRK or LASIK) unless need for possible transplant is understood and accepted



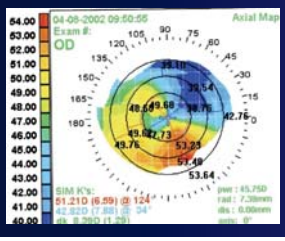
Keratoconus & Pellucid Degenerations

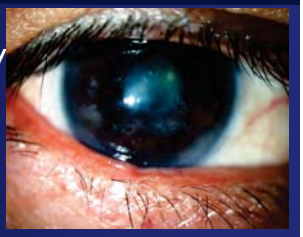
- Surgical management
  - Intacs
    - Stabilize cornea and reduce irregular astigmia & myopia
    - Keratoconus or Pellucid

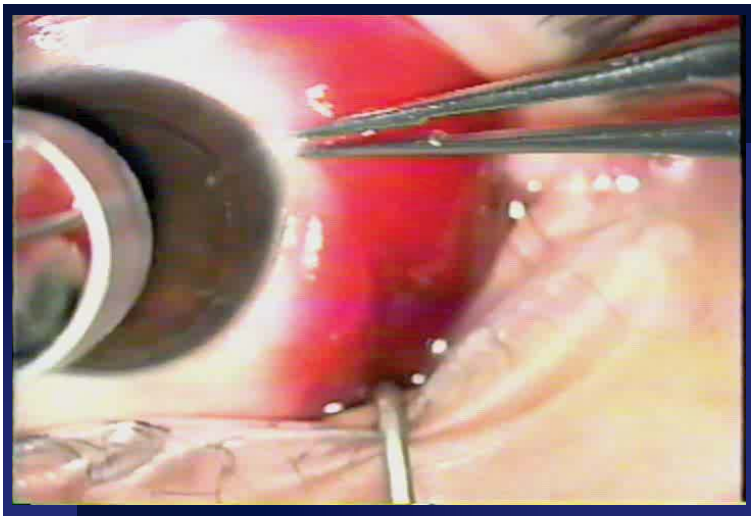


Keratoconus & Pellucid Degenerations

- Surgical Management
  - Anterior Lamellar Keratectomy (ALK, aka DALK)
  - Penetrating Keratoplasty (PK)

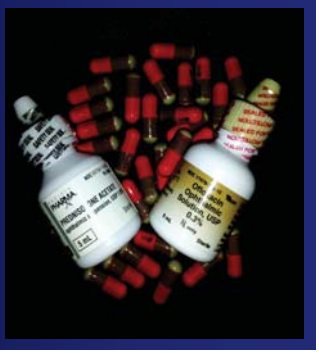






Keratoconus & Pellucid Degenerations

- Postop comanagement DALK
  - Medication
  - Leaks (none expected)
  - Shield
  - Restriction



Keratoconus & Pellucid Degenerations

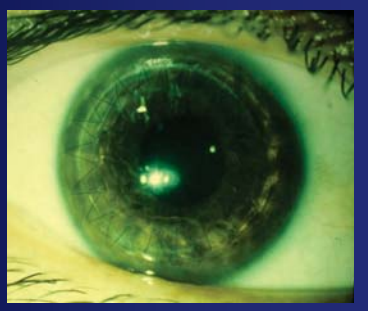
- **Postop comanagement DALK**
  - **Follow-up**
    - 1 day
    - 1 week
    - 3 to 6 weeks
    - 6 to 12 weeks
      - Sutures out
    - 6 months
    - 12 months
    - Rejection least likely of transplant procedures

Keratoconus & Pellucid Degenerations

- **Surgical management**
  - **Penetrating Keratoplasty (PKP)**

Keratoconus & Pellucid Degenerations

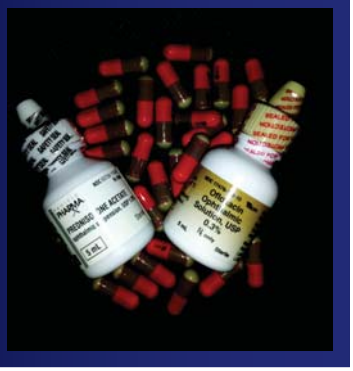
- **Surgical management**
  - **Running suture**
  - **Interrupted sutures**



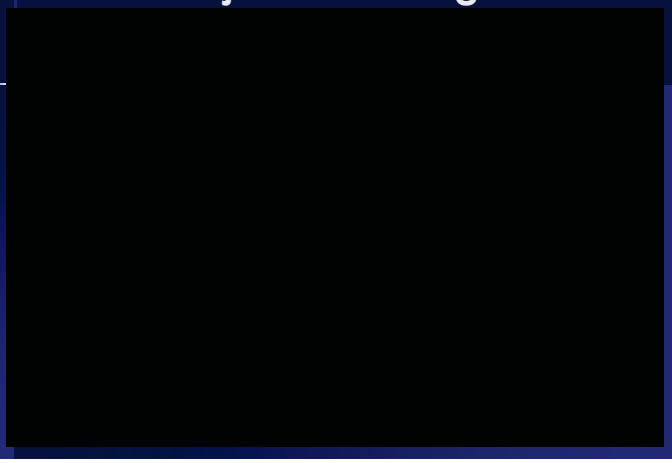
Secondary Penetrating Keratoplasty

Keratoconus & Pellucid Degenerations

- **Post op PKP comanagement**
  - **Medication**
  - **Shield (2w bedtime)**
  - **Leaks**
  - **Suture adjustment and removal**
    - Early adjustment important
    - Running suture remains 12m
    - Interrupted sutures out by 6m
  - **Restriction**
    - 2w off work
    - No lifting over 25 lbs 6w



Suture Adjustment Astigmatism



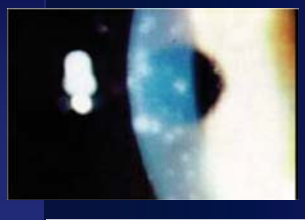
Suture Adjustment Seidel

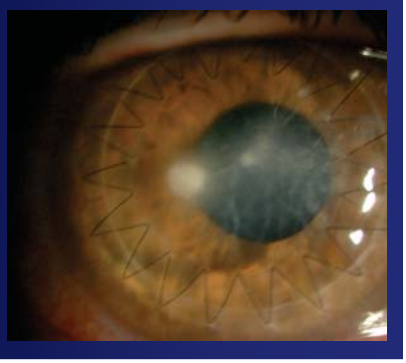
Keratoconus & Pellucid Degenerations

- **Post op PK comanagement**
  - **Follow-up:**
    - 1 day
    - 1 week
    - 2 – 4 week
    - TBD
    - Watch for steroid related IOP rise
    - Watch for rejection

Keratoconus & Pellucid Degenerations

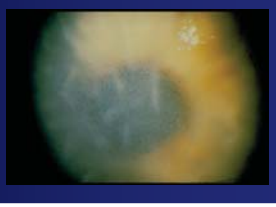
- **Post op PK comanagement**
  - **Follow-up:** Watch for infection





Fuchs' Dystrophy

- **Diagnostic Features**
  - **Abnormal endothelium:**
    - shape, size and number
  - **Corneal edema**
    - Early, deep stromal
    - Late, stromal and epithelial
  - **Visual blur late**
  - **Epithelial edema then bullous keratopathy late**
  - **Irritation to pain**



Fuchs' Dystrophy

- **Diagnostic Features**
  - **Corneal edema**
    - Late, stromal and epithelial
  - **Visual blur late**

Fuchs' Dystrophy

- **Impact on cataract management**
  - **Decision for cataract extraction**
    - Severity of cataract
    - Relative contributions to reduced VA
    - Related ocular discomfort or pain
    - Impact of concurrent glaucoma
    - Life expectancy
  - **Cataract only**
    - Viscoelastic
  - **Triple procedure**
    - (PKP, PLK or DMEK, CE c IOL)

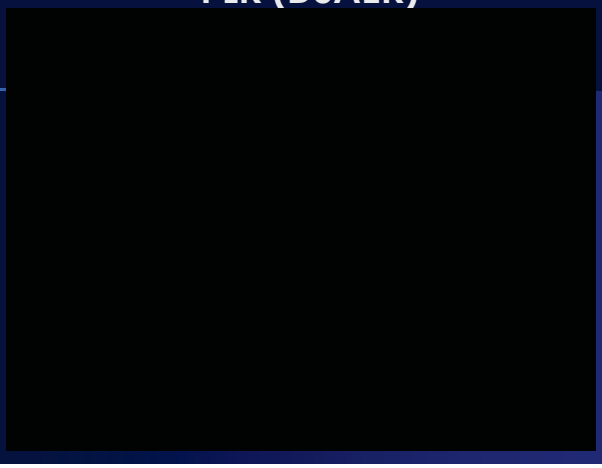
Fuchs' Dystrophy

- Surgical management
  - Descemet's Stripping Automated Endothelial Keratoplasty (DSAEK or PLK)
  - Descemet's Membrane Endothelial Keratoplasty (DMEK)

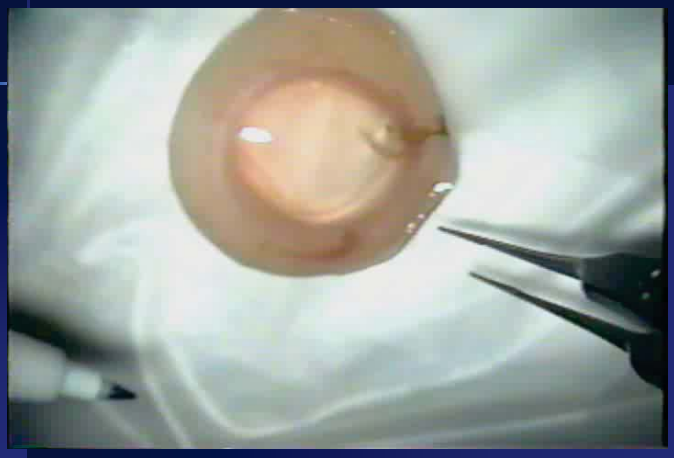
Fuchs' Dystrophy

- Surgical management
  - DSAEK or DMEK
    - Newer approaches to corneal clouding and painful edema secondary to endothelial dysfunction
    - Advantages relative to PKP
      - Faster recovery
      - Better post op structural integrity
        - More resistant to perforation / rupture
        - Ocular surface: Yes & No
        - Better optics
      - Similar risk for rejection ?
      - Probably lower risk of infection

PLK (DSAEK)



PLK SURGERY (DMEK)

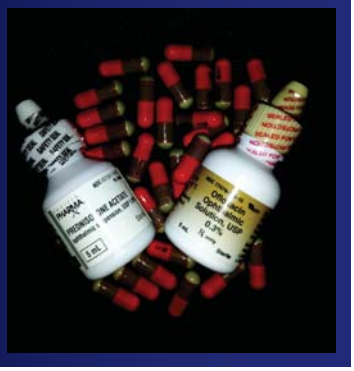


PLK One Day Post Op

PLK 2 Months Post Op

Fuchs' Dystrophy

- **Post op DSAEK/DMEK comanagement**
  - **Medication**
  - **Shield**
  - **Leaks**
  - **Restriction**



Fuchs' Dystrophy

- **Post op DSAEK/DMEK comanagement**
  - **Follow-up:**
    - 1 day
    - 1 week
    - 2 – 4 week
    - Watch for pupil block
    - Vigilance for graft mal-position (early)
    - Watch for steroid related IOP rise
    - Watch for rejection
  - **Patient expectation**

Thank You

UPCOMING EVENTS

Tulalip CE
Sunday, September 18
Tulalip Casino Resort
6 hours of CE, $250

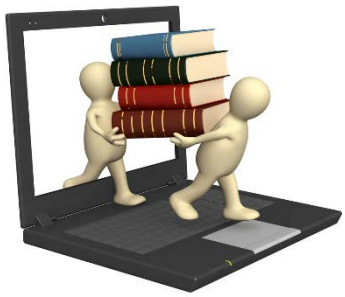
GWCO – Join us for our annual "Bus CE Event", Saturday, October 1
Take a ride out to Pacific University and be challenged with cases from Lorne Yudcovitch and James Kundart. Refreshments and a tour of the College of Optometry is included. This event is included with your registration to GWCO.

Homecoming CE – Saturday, October 15, 2016,
Pacific University Jefferson Hall
"The Ocular Surface and More"
5 hours of CE, $100
John Clement, Tracy Doll, Derek Louie, Jeong Kim

Glaucoma Symposium – Saturday, January 14, 2017
Woodinville, Washington, 6 hours of CE featuring Howard Barnebey and Murray Fingeret.
For more information contact: frederim@pacificu.edu

2017 ISLAND EYES CONFERENCE
January 22 – 28, 2017
Kauai Marriott Resort
Up to 31 hours of education
Pat Caroline, Bradley Coffey, David Kading, Nate Lighthizer, Danica Marrelli, Lorne Yudcovitch and Robert Reed
For more conference Information contact: JEANNE@pacificu.edu

Can't make it to a meeting? We offer 1, 2 & 3 credit classes online.
https://online-ce.opt.pacificu.edu/



2016 VICTORIA CONFERENCE

EVALUATION

Please circle how well the speaker met the stated learning objectives

Thursday, July 21, 2016	1	Kathleen Elliott, "Pediatrics/Geriatrics" *Based on this lecture, what would you take back to your practice?*	5	4	3	2	1
	2	Jeff Urness, "Corneal Conditions and Refractive Surgery" *Based on this lecture, what would you take back to your practice?*	5	4	3	2	1
	3	Amber Giannoni, "Environment, Diet & Supplements" *Based on this lecture, what would you take back to your practice?*	5	4	3	2	1
Friday, July 22, 2016	4	Amber Giannoni, "Dry Eye and Systemic Disease" *Based on this lecture, what would you take back to your practice?*	5	4	3	2	1
	5	Kathleen Elliott, "ABC's of Pediatric Eye Care" *Based on this lecture, what would you take back to your practice?*	5	4	3	2	1
	6	John McGreal, "New Ideas in Glaucoma Management" *Based on this lecture, what would you take back to your practice?*	5	4	3	2	1
Saturday, July 23, 2016	7	John McGreal, "Latest Trends in Contemporary Medicine" *Based on this lecture, what would you take back to your practice?*	5	4	3	2	1
	8	Kathleen Elliott, "Periocular Soft Tissue Rejuvenation" *Based on this lecture, what would you take back to your practice?*	5	4	3	2	1
	9	John McGreal, "New Tools for the Toolbox" *Based on this lecture, what would you take back to your practice?*	5	4	3	2	1

Please complete both sides of this form and return to the conference administrator at the conclusion of the conference.

2016 VICTORIA CONFERENCE

EVALUATION

Please circle how well the speaker met the stated learning objectives

Sunday, July 24, 2016	10	Jeff Urness, "Bacterial Corneal Ulcers" *Based on this lecture, what would you take back to your practice?*	5	4	3	2	1
	11	Kathleen Elliott, "Pediatric Case Reports" *Based on this lecture, what would you take back to your practice?*	5	4	3	2	1
	12	Amber Giannoni, "Setting Up a Dry Eye Practice" *Based on this lecture, what would you take back to your practice?*	5	4	3	2	1
	13	Jeff Urness, "Corneal Transplantation" *Based on this lecture, what would you take back to your practice?*	5	4	3	2	1

	14	Delta Victoria Ocean Point Resort Property *Comments*	5	4	3	2	1
	15	Delta Victoria Ocean Point MEETING ROOMS *Comments*	5	4	3	2	1
	16	Pacific University Conference Staff *Comments*	5	4	3	2	1
		OTHER COMMENTS and speaker or topic recommendations					

Please complete both sides of this form and return to the conference administrator at the conclusion of the conference.