EVERYTHING THERAPEUTIC

CourseMaster
Bruce Onofrey, RPh, OD, FAAO

June 20-21
2015

4811 Calhoun Road, Houston, TX 77204-2020
Saturday, June 20, 2015

7:00 am - 8:00 am  Registration/Continental Breakfast/Visit Exhibits

Lectures presented by Alan Kabat, OD:

8:00 am - 9:45 am  Unraveling the Enigma of Ocular Surface Disease  COPE ID# 42088-AS
9:45 am - 10:15 am  Break/Visit Exhibits
10:15 am - 12:00 pm  Pill Problems: Ocular Complications from Systemic Medications  COPE ID# 35069-OP
12:00 pm - 1:00 pm  Lunch/Visit Exhibits

Lectures presented by Emmanuel Chang, MD, PhD:

1:00 pm - 1:50 pm  Retinal Vascular Diseases and Diabetes – Is there even a role for Laser Anymore?  COPE ID# 44959-PS
1:50 pm - 2:40 pm  Pediatric Retinal Diseases – What did I miss there?  COPE ID# 44955-PS
2:40 pm - 3:10 pm  Break/Visit Exhibits
3:10 pm - 4:05 pm  AMD/Puckers/Holes – You can Surgically do what to the Macula?!  COPE ID# 44956-PS
4:05 pm - 5:00 pm  The Future of AMD – What do I need to know on the Horizon?  COPE ID# 44957-PS

Sunday, June 21, 2015

7:00 am - 8:00 am  Registration/Continental Breakfast/Visit Exhibits

Lectures presented by Joseph Sowka, OD:

8:00 am - 9:45 am  The Clinicians Guide To Glaucoma: Managing Cases and Complexities  COPE ID# 38871-GL
9:45 am - 10:15 am  Break/Visit Exhibits
10:15 am - 12:00 pm  Diagnosing and Management of Neuro-Ophthalmic Diseases  COPE ID# 34967-NO
12:00 pm - 1:00 pm  Lunch/Visit Exhibits

Lecture presented by Nathan Lighthizer, OD:

1:00 pm - 2:40 pm  VEP & ERG: Electrodiagnostics in Clinical Practice: Patient Wins, Practice Wins  COPE ID# 44905-PD
2:40 pm - 3:10 pm  Break/Visit Exhibits

Lecture presented by Jim Owen, OD, MBA, FAAO:

3:10 pm - 4:00 pm  New Innovations in Surgical Eye Care  COPE ID# 44889-RS

Lecture presented by Bruce Onofrey, RPh, OD, FAAO:

4:00 pm - 5:00 pm  2015 Professional Responsibility Course  COPE ID# 44900-EJ
**UNRAVELING THE ENIGMA OF OCULAR SURFACE DISEASE**

ALAN G. KABAT, OD, FAAO*

[Email link]

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**Course Description:** Ocular surface disease encompasses a wide range of conditions, including dry eye disease, blepharitis, ocular allergy and many other lesser known entities. This course presents a clinically relevant overview of ocular surface disorders with practical management strategies.

**Learning Objectives/Outcomes:** At the conclusion of this course, the attendee will be able to:

1. Outline and discuss a working definition for the broad category of disorders now known as ‘ocular surface disease’ (OSD);
2. Differentiate the various forms of dry eye – aqueous deficient, evaporative and mechanical – identifying their respective etiologies;
3. Differentiate the various forms of blepharitis and identify their causative elements, including microscopic and macroscopic organisms;
4. Understand the role that ocular allergy plays in OSD;
5. Identify a diagnostic algorithm for approaching OSD, understanding the role and clinical value of each test;
6. Identify a sound management strategy for each of the contributory aspects of OSD.

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**Definition of OSD**


**Conditions that alter the production, composition, or distribution of the preocular tear film may result in symptoms or signs of damage to the structures of the ocular surface. These situations may lead to noticeable irritation, reduction of visual function, and even chronic tissue changes. Such conditions are often related to abnormalities of the structure or function of the eyelids, glands of the lid and their secretions, conjunctiva and/or cornea.**

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* Dr. Alan Kabat is Professor at Southern College of Optometry and Clinical Care Consultant at TearWell Advanced Dry Eye Treatment Center in Memphis, Tennessee. Dr. Kabat is a paid consultant for Alcon Laboratories and Bio-Tissue; in addition, he serves on clinical advisory boards for TearScience and Nicox.
Contributory elements of OSD:

- Aqueous-deficient dry eye
  - Sjögren's syndrome
  - Non-Sjögren's aqueous deficiency (e.g., age-related)
  - Post-surgical disruptions of the ocular surface and tear film
- Evaporative dry eye
  - Situational and environmental evaporative tear loss
  - Blink and lid anatomy abnormalities
  - Contact lens-related evaporative tear disruption
- Blepharitis
  - Anterior (lash- and lid-associated)
    - Demodiconis
  - Posterior (lid margin- and meibomian gland-associated)
- Mechanical abnormalities
  - Conjunctivochalasis (redundant bulbar conjunctival tissue)
  - Anterior corneal dystrophies and irregularities
- Allergic conjunctivitis and keratoconjunctivitis
- Chronic infectious conjunctivitis and keratoconjunctivitis
- Chronic non-infectious conjunctivitis and keratoconjunctivitis

OSD: Diagnostic technology

- Questionnaires
  - Standard Patient Evaluation of Eye Dryness = SPEED
  - Ocular Surface Disease Index = OSDI
- TearLab® = tear osmolarity (osmolality)
- LipiView®
  - QUANTITATIVE lipid layer assessment
  - Also reveals blink dynamics (number, frequency, complete vs. incomplete)
- InflammaDry® = inflammatory biomarker (matrix metalloproteinase-9 or MMP-9)
- OCULUS Keratograph 5M
  - Non-invasive Keratograph break-up time = NIKBUT
  - Tear meniscus height
  - QUALITATIVE lipid layer assessment
  - Infrared meibography
- ZoneQuick® and Schirmer test = assessment of tear volume
- Slit lamp evaluation, with particular attention to:
  - Lagophthalmos
  - Lid margin assessment
    - Margin redness/inflammation
    - Lashes and associated debris
    - Cylindrical dandruff, indicative of Demodex
    - Meibomian orifices
    - Line of Marx (lissamine green)
Tear film quantity, quality & debris (subjective)

Conjunctival assessment (including lissamine staining)
- Redness
- Chemosis
- Lid-parallel conjunctival folds (LIPCOF), or conjunctivochalasis (CCh)

Corneal assessment (including sodium fluorescein and lissamine staining)
- Surface regularity
- Surface wetting
- Epithelial disruption
- Stromal irregularities or deposits
- Endothelial integrity

- Meibomian gland transillumination
- STANDARDIZED meibomian gland expression (MGE)
- Eyelash epilation and microscopy for Demodex

- SjÖ = serum biomarkers for Sjögren syndrome
- Doctor’s Allergy Formula® Testing = identification of sensitivity to ocular-specific allergens

OSD: Differential Diagnoses (most commonly used diagnoses in TearWell)
- Allergic conjunctivitis [372.14]
- Aqueous deficient dry eye disease [375.15] & keratoconjunctivitis sicca [370.33]
- Epithelial basement membrane dystrophy/disease/dysfunction (EBMD) [371.52]
- Anterior blepharitis [373.00]
- Posterior blepharitis ≈ meibomian gland dysfunction (MGD) [373.00]
- Blink lagophthalmos and nocturnal lagophthalmos [374.20]
- Conjunctivochalasis [372.81]
- Demodicosis (Demodex folliculorum [133.8] & parasitic infestation of lid [373.6])

Allergic conjunctivitis

- Key diagnostic features and findings
  - Ocular itching
    - Worsens after rubbing!
  - Eyelid and periocular edema
  - Hyperemia and chemosis of caruncle, plica and bulbar conjunctiva
  - Positive history of atopy and other atopic disorders (e.g. asthma, eczema)

- Adjunctive testing
  - Tear IgE (Advanced Tear Diagnostics, Birmingham, AL) ?
  - Doctor’s Allergy Formula® Testing

- Management strategies
  - Avoidance
  - Topical OTC drugs (vasoconstrictor/antihistamine, antihistamine/mast cell stabilizer)
  - Topical Rx drugs (antihistamine/mast cell stabilizer, corticosteroid, NSAID)
o Oral Rx drugs (antihistamine, corticosteroid)
  o Nasal Rx drugs (antihistamine/mast cell stabilizer, corticosteroid)

**Aqueous deficient dry eye disease / keratoconjunctivitis sicca**

- **Key diagnostic features and findings**
  - Variable symptoms... burning, grittiness, eyelid “sticking”, etc.
  - Symptoms usually worse at the END of day or with prolonged visual tasking (TV, computer, driving, reading)
  - Variable ocular hyperemia
  - Variable corneal staining (sodium fluorescein and/or lissamine green)
  - Variable conjunctival staining (lissamine green)
  - Diminished tear meniscus (aka tear prism) and/or measured tear volume
  - Diminished tear break-up time

- **Adjunctive testing**
  - Vital dye staining
  - InflammaDry
  - Tear volume assessment (e.g. Schirmer, ZoneQuick®)
  - SJÖ®

- **Management strategies**
  - Restasis®
    - +/- corticosteroid induction therapy (i.e. Lotemax®)
    - HOW LONG?
  - Oral omega-3 (EFA) dietary supplements
  - Oral cholinergic agents (e.g. pilocarpine, cevimeline)
    - Stimulate aqueous production
    - OFF-LABEL for dry eye
    - Should ONLY be used upon consultation with rheumatology
  - Supplemental artificial tears, depending upon severity
    - Preserved vs. preservative-free
    - Viscosity
    - Time-release agent, e.g. Lacrisert®

**EBMD**

- **Key diagnostic features and findings**
  - Symptoms worse upon awakening
  - Irregular “map-like” pattern upon sodium fluorescein instillation
  - Classic “map-dot-fingerprint” presentation
  - Rapid or immediate tear break up over “map-like” areas

- **Adjunctive testing**
  - Vital dye staining
  - External photography
  - Corneal topography

- **Management strategies**
Lubrication therapy
- FreshKote®
- NaCl 5-10% solution or ointment
- Hair dryer
- Manage recurrent corneal erosion
- PTK?

**Anterior blepharitis**

- Key diagnostic features and findings
  - Gritty, sandy feeling
  - Symptoms worse upon awakening
  - Crust, brittle, fibrinous scales along lash base
  - Erythematous lids
  - Possible inferior PEK
- Adjunctive testing
  - Empirical... rule out demodicosis
- Management strategies
  - Lid cleansing / lid hygiene
  - Topical antibiotic or antibiotic/corticosteroid
  - Lubrication therapy
    - Lipid-restorative solution (e.g. Systane® Balance, retaine® MGD, etc.)

**MGD**

- Key diagnostic features and findings
  - Burning sensation of eyes is common; typically worse upon awakening or with prolonged visual tasking (TV, computer, driving, reading)
  - Diminished meibomian gland expressibility and fluidity of secretions
  - Meibomian gland orifice inspissation and dysplasia (variable)
  - Meibomian gland dropout (variable)
  - Lid margin hyperemia, thickening
  - Displaced Line of Marx (anterior)
  - Diminished tear break-up time
  - Possible inferior PEK
- Adjunctive testing
  - LipiView®
  - Infrared meibography / meibomian gland transillumination
  - Meibomian gland expression (diagnostic)
- Management strategies
  - Lid hyperthermia / gland expression
    - Patient-initiated
    - Doctor-facilitated (IPL, “cold expression”)
    - Automated (i.e. LipiFlow®)
  - Oral omega-3 (EFA) dietary supplements
o Oral tetracycline derivatives (meibomian gland inflammation modulators)
o Lubrication therapy
  ▪ Lipid-restorative solution (e.g. Systane® Balance, retaine® MGD, etc.)

Lagophthalmos

• Key diagnostic features and findings
  o Sandy, gritty feeling, often upon awakening
    ▪ Worsens with decreased humidity or increased airflow
  o Incomplete blink noted on evaluation
  o History of “sleeping with eyes open”
  o Possible inferior PEK
• Adjunctive testing
  o LipiView®
  o Vital dye staining
• Management strategies
  o Blink training (exercises)
  o Ocular lubricants
  o Ophthalmic ointments and gels for overnight therapy
  o Protective eyewear (“sleep mask”) for overnight therapy

Conjunctivochalasis

• Key diagnostic features and findings
  o Redundant conjunctiva, noted as lid-parallel folds on biomicroscopy
    ▪ Usually more prominent temporally
    ▪ Usually more evident in downgaze (disappear in upgaze)
• Adjunctive testing
  o Vital dye staining (lissamine green >> sodium fluorescein)
• Management strategies
  o Few non-invasive therapies are particularly helpful
    ▪ Lubrication therapy
    ▪ Possible corticosteroid
  o Ultimately, conjunctival resection is indicated
    ▪ “Paste-pinch-cut” conjunctivoplasty

Demodicosis

• Key diagnostic features and findings
  o Ocular surface and eyelid irritation
    ▪ Variable response & interpretation (itching, burning, grittiness, etc.)
    ▪ Generally worse in the evening (greater motility of organisms)
  o Hyperemic conjunctiva and/or lids
  o Cylindrical dandruff on lashes
• Adjunctive testing
  o Forceps manipulation/epilation
Microscopic evaluation of eyelashes & lid debris
External photography

Management strategies
Tea tree oil considered most effective treatment
- Concentration? Application?
- Cliradex
Regimen of continuous lid hygiene

Recommended reading:

PILL PROBLEMS: OCULAR COMPLICATIONS FROM SYSTEMIC MEDICATIONS

Course description: This course presents current information about common oral prescription medications and their ocular complications and manifestations. The use of case examples and series culled from the literature highlight and reinforce the instructional objectives.

Learning Objectives/Outcomes: At the conclusion of this lecture, the attendee will be able to:

1. Recognize the ocular and non-ocular complications associated with oral diphenhydramine.
2. Recognize the ocular and non-ocular complications associated with oral hydrochloroquine.
3. Recognize the ocular and non-ocular complications associated with oral sildenafil.
4. Recognize the ocular and non-ocular complications associated with oral tamsulosin.
5. Recognize the ocular and non-ocular complications associated with oral warfarin.
6. Recognize the ocular and non-ocular complications associated with oral topiramate.

- **Common Drugs with Ocular Complications**
  - Alendronate
  - Amiodarone
  - Benztropine
  - Diphenhydramine
  - Hydroxychloroquine
  - Sildenafil
  - Tamsulosin
  - Tetracycline
  - Topiramate
  - Warfarin

- **DIPHENHYDRAMINE**
  - Trade: Benadryl®, numerous generic
  - Drug class: non-selective histamine blocker
    - Ingredient in numerous cold medications and sleep aids (e.g. Nytol®, Tylenol® PM)
Indication(s):
- Primary: nasal & non-nasal signs and symptoms of seasonal allergy, especially allergic rhinitis
- Secondary: insomnia, vertigo, motion sickness

Typical dosage: 25-50 mg, q4h or PRN

Ocular Complications
- Dry Eye
  - Due to anticholinergic effects of the medication
  - Diminishes aqueous production via autonomic innervation to the primary lacrimal gland
  - Opposite action of Salagen® (pilocarpine)
- Can also cause dry mouth, urinary retention and constipation
- Dose-dependent effect
- Reversible

- ... to evaluate the safety of olopatadine 0.2% in a population of patients with both allergic conjunctivitis and dry eye.
- 52 patients with ocular allergy and mild-to-moderate dry eye were evaluated.
- Randomized to either olopatadine hydrochloride 0.2% or a tear saline once-daily for 1 week.
- Evaluated TBUT, corneal and conjunctival staining, fluorophotometry, Schirmer's test, injection, and symptom evaluations.
- No significant differences between the treatment groups were observed (p > 0.05).

**Conclusion:** As there were no significant changes in the signs & symptoms of dry eye, olopatadine 0.2% is safe to use in ocular allergy patients with mild-to-moderate dry eye.

Other Manifestations
- Drowsiness & fatigue
- Anticholinergic effects including dry mouth, urinary retention, and constipation
- Potential for cardiac complications, particularly arrhythmias and tachycardia
- Potential for recreational use/abuse

Similar Medications with Similar Effects
- Chlorpheniramine (Chlor-Trimeton®)
- Brompheniramine (Dimetane®)
- Dimenhydrinate (Dramamine®)
- Meclizine (Bonine®)
- Loratadine (Claritin®, Alavert®)
- Cetirizine (Zyrtec®)
• OTC vs. Rx Drugs: Patients do not always equate items that they buy on store shelves with the terms “drugs” or “medications”. Practitioners and technicians must be SPECIFIC when screening. Checklists on intake forms work well.

• TETRACYCLINE and derivatives
  – Trade: Sumycin®, Tetracyn®, numerous generics
  – Drug class: Tetracycline antibiotic
  – Includes doxycycline and minocycline, among others
  – Indication(s):
    ▪ Primary: infection by susceptible bacterial strains
      • Respiratory, skin/soft tissue, UTIs most commonly
      • Rarely a “first-line” antibiotic therapy
    – Secondary: immunomodulatory agent for sebaceous disorders, including rosacea and MGD
  – Typical dosage: 250 mg QID or 500 mg BID
  – Ocular Complications
    ▪ Scleral discoloration (minocycline)
    ▪ Pseudotumor cerebri or Idiopathic intracranial hypertension
      • 0.9 per 100,000 people in general population, including children
      • Increased risk in women aged 20-44 who are 20% or more above their ideal body weight
    ▪ Diagnosis - based on modified Dandy criteria
      ♦ Awake and alert patient
      ♦ Signs and symptoms of increased ICP
      ♦ Absence of localized neuro exam findings, except for CN VI paresis
      ♦ Normal CSF fluid findings except for increased pressure
      ♦ Absence of deformity, displacement, and obstruction of ventricular system
      ♦ No other identifiable cause of intracranial hypertension

• Other compounds associated with PTC
  • Oral contraceptives
  • Vitamin A
  • Amiodarone
  • Glucocorticoids (withdrawal)
  • Mineralocorticoids (withdrawal)
• Other Manifestations
  • Tooth Discoloration
  • Photosensitivity
• WARFARIN
  – Trade: Coumadin®, numerous generics
  – Drug class: anticoagulant (“blood thinner”)
  – Indication(s):
    ▪ Prophylaxis and/or treatment of venous thrombosis and pulmonary embolism
    ▪ Thromboembolic complications associated with atrial fibrillation and/or cardiac valve replacement
    ▪ To reduce the risk of death, recurrent myocardial infarction, and thromboembolic events such as stroke or systemic embolization after myocardial infarction
    ▪ Hypercoagulable states
  – Typical dosage: 5-10 mg daily

  – Ocular Complications
    ▪ Subconjunctival hemorrhage
    ▪ Hyphema
    ▪ Retinal hemorrhage
  – Other Manifestations
    ▪ Bleeding and bruising - can be potentiated by a variety of drugs & other substances:
      • Antibiotics (e.g. aminoglycosides, macrolides, fluoroquinolones and tetracyclines)
      • Beta-blockers
      • Levothyroxine
      • Atorvastatin
      • Fish oil / Ω-3 / vitamin E
      • Alcoholic beverages
      • Cranberry products
      • Ginseng
      • Garlic
      • Ginko biloba
      • St. John’s wort
  – Management Tips
    ▪ Patients on warfarin therapy need to be cognizant of everything they put in their mouths. Medications, food, beverages... EVERYTHING!!
    ▪ INR (International Normalized Ratio) should be performed by PCP routinely.
    ▪ Measures the extrinsic pathway of coagulation
    ▪ Normal: 0.8 – 1.2
    ▪ Target range on therapy: 2.0 – 3.0
    ▪ Dangerous: >4.0
• AMIODARONE
  – Trade: Cordarone®, Pacerone®, numerous generics
  – Drug class: anti-arrhythmic agent (Class III)
  – Indication: for life-threatening cardiac arrhythmias
    ▪ hemodynamically unstable ventricular tachycardia
    ▪ shock-resistant, recurrent ventricular fibrillation
  – Typical dosage: 200-400 mg/day

  – Ocular Complications
    ▪ Corneal Verticillata
    ▪ i.e. “vortex keratopathy”, “hurricane keratopathy”
      • Generally asymptomatic
      • Rarely may cause haloes or slight decrease in VA
      • Seen in ~90% of patients on amiodarone >6 mos, especially those taking >400 mg/day.
      • No management required; Self-limiting & reversible
    • WARNING: Vortex keratopathy can also be associated with FABRY’S DISEASE
      ♦ Hereditary enzyme deficiency
      ♦ α-Galactosidase A
      ♦ located on the X-chromosome
      ♦ Leads to intracellular accumulation of neutral glycosphingolipids in various organs, e.g. skin, eyes, nervous tissue, kidney and heart
      ♦ Findings: angiokeratomas, pain in the hands & feet, lesions of the mouth and multiple ocular signs
      ▪ Pseudotumor cerebri or Idiopathic intracranial hypertension
  – Other Manifestations
    ▪ “Blue skin”, “blue man syndrome”
    ▪ Long-term use; more commonly seen with lighter skin tones

• TOPIRAAMATE
  – Trade: Topamax®
  – Drug class: anticonvulsant
  – Indication(s):
    ▪ Primary: treatment of epilepsy and other seizure disorders
    ▪ Secondary: prevention of migraine headaches in adults
    ▪ Off-label: treatment of bipolar disorder, obsessive-compulsive disorder, alcoholism, smoking cessation, cocaine dependence, eating disorders, and neuropathic pain.
  – Typical dosage: (adults) 100 – 400 mg daily
Ocular Complications
  - Acute myopic shift
  - Acute angle-closure glaucoma
  - Pathological Mechanism
    - Appears to be a sulfa-allergic response
    - Swelling/congestion and forward rotation of the ciliary body
    - Ciliochoroidal effusion with forward shifting of lens-iris diaphragm
    - Induces extreme anterior chamber shallowing and angle-closure
    - Congestion of ciliary body allows lens zonules to go slack
      - Results in lens thickening; this, in addition to the forward rotation of the lens-iris diaphragm induces a myopic shift
      - Lens thickening generally does not contribute to angle closure
    - NO pupil block; NO iris bombé!
  - Cyclocongestive glaucoma
    - Normal open angle
    - Cyclocongestive angle closure

Other Manifestations
  - Dysgeusia (taste perversion)
  - Parasthesias (numbness & tingling)
  - Fatigue
  - Difficulty with concentration, attention and memory
  - Weight loss

TAMSULOSIN
  - Trade: Flomax
  - Drug class: alpha-adreneric antagonist
  - Indication(s):
    - Primary: signs and symptoms of benign prostatic hyperplasia (BPH)
    - Off label: urinary retention in women and those with multiple sclerosis; facilitated passage of kidney stones
  - Typical dosage: 0.4 mg once daily
  - Mechanism: works by relaxing smooth muscle at the distal portion of the urethra
  - Ocular Complications
    - IFIS - Intra-operative Floppy Iris Syndrome
    - Clinical manifestations:
      - Poor preoperative dilation
      - Iris billowing and prolapse
      - Progressive intraoperative miosis
Management:
- Identify patients at risk and discontinue medication if possible
- Use of stronger dilating agents, e.g. epinephrine and/or atropine
- Use of Malyugin or Morcher ring

Other Manifestations
- Sulfa Allergy
- Pustular, erythematous skin eruptions with urticaria
- Can affect any part of the body
- May progress to Stevens-Johnson syndrome in severe cases
- Fever, chills, body aches, or flu symptoms
- Light headedness, dizziness, weakness, drowsiness
- Headache
- Nausea, diarhhea
- Runny nose
- Diminished ejaculate
- Decreased sex drive, which leads us to...

**SILDENAFIL**
- Trade: Viagra®
- Similar medications: tadalafil (Cialis®), vardenafil (Levitra®, Staxyn®)
- Drug class: phosphodiesterase enzyme inhibitor (PDEI)
- Originally studied as an anti-angina medication!
- Indication(s):
  - Primary: treatment of erectile dysfunction
  - Secondary: symptoms of benign prostatic hyperplasia
  - Off-label: pulmonary hypertension, Raynaud's phenomenon (Revatio®)
- Typical dosage: 50 mg (not to exceed 100 mg)

Mechanism of action (warning: GRAPHIC)
- Ocular Manifestations
  - Cyanopsia (“blue vision”)
    - By affecting PDE6 in the retina, sildenafil can lead to altered color vision perception (usually a blue or green “tinge” to vision).
    - 4 out of 5 men without vascular risk factors reported this problem after taking sildenafil.
  - Nonarteritic anterior ischemic optic neuropathy
- Other Manifestations
  - Headache
  - Stuffy nose
  - Facial flushing
- Other Manifestations

- HYDROXYCHLOROQUINE
  - Trade: Plaquenil®, numerous generic
  - Drug class: aminoquinoline
    - anti-malarial drug
    - DMARD
  - Indication(s):
    - treatment of malaria
    - treatment of discoid and systemic lupus erythematosus, and rheumatoid arthritis
  - Typical dosage: 400-800 mg/day (malaria); 200-400 mg/day (lupus & RA)

- Ocular Manifestations
  - Corneal deposits
  - “Bulls-eye” maculopathy
  - 66 visual fields from patients with HCQ retinal toxicity.
  - HVF changes preceded fundus changes in 60% of patients.
  - Abnormalities were more obvious on pattern deviation than the gray scale.
  - Authors recommend white stimulus 10-2 fields (vs. red-stimulus), as per AAO guidelines.
  - OCT: The New Standard


- OCT: The New Standard
  - Focal thinning and loss of parafoveal PIL (photoreceptor integrity line)

- ERG: The Emerging Standard

- Risk factors for maculopathy
  - Maintenance dose greater than 6.5 mg/kg/d
  - 120 lb. woman: >400 mg/d
  - 200 lb. man: >600 mg/d
  - Duration of treatment: >10 years
- Evidence of renal insufficiency or hepatic disease
- Obesity
- Advanced age
- Presence of macular degeneration or dystrophy
  - Other Manifestations
    - Vertigo, tinnitus, headache
    - Skin rashes and dermatitis
    - GI disturbances
    - Muscle weakness

- **ALENDRONATE**
  - Trade: Fosamax®, numerous generic
  - Drug class: aminobiphosphonate
    - anti-resorptive agent (strengthens bones)
    - similar drugs include Actonel®, Boniva®
  - Indication(s):
    - Primary: treatment or prevention of osteoporosis, treatment of Paget’s disease
    - Off label: Metastatic bone cancer, hypercalcemia, vitamin D overdose
    - Typical dosage: 5-10 mg/day (osteoporosis); 40 mg/day (Paget’s disease) X 6 months
  - Ocular Manifestations
    - Non-specific conjunctivitis and/or keratitis
  - Other Manifestations
    - Nausea, dyspepsia, acid regurgitation
    - Abdominal pain, constipation, diarrhea
    - Musculoskeletal pain
    - Hypocalcemia
    - Osteonecrosis of the jaw

- **BENZTROPINE**
  - Trade: Cogentin® (discontinued in US); numerous generics
  - Drug class: anti-parkinsonian medication
  - Possesses both anticholinergic and antihistaminic effects
  - Indication(s):
    - As an adjunct in the therapy of all forms of Parkinsonism
    - For control of medication-induced movement disorders due to antipsychotic agents, e.g. chlorpromazine (Thorazine®), haloperidol (Haldol®), risperidone (Risperdal®), olanzapine (Zyprexa®), quetiapine (Seroquel®)
  - Typical dosage: 1-2 mg/day
- Ocular Manifestations
  - Anticholinergic effects (think atropine!):
    - Mydriasis
    - Cycloplegia
    - Impaired accommodation
    - Transient refractive shift
  - Dry eyes
  - Esotropia / diplopia
    - Proposed mechanism: *The ratio of convergence to accommodation may increase with anticholinergics due to partial block of accommodation. To see a near target in the setting of blocked accommodation, children would increase accommodative effort, resulting in increased convergence. Too much convergence may cause esotropia.*
- Other Manifestations
  - MORE anticholinergic effects

- CONCLUSIONS:
  - Optometric PHYSICIANS must realize that the eye is impacted by numerous systemic diseases and drugs.
  - A working knowledge of pharmacology and common drugs is essential (especially when dealing with an adult or geriatric population).
  - Even if you don’t (or can’t) prescribe them, you have the responsibility to recognize the potential ocular impact of commonly prescribed medications.
Venous vascular caliber and tortuosity is governed by perfusion and intraocular VEGF levels and blood outflow compromise. Arterial vascular tortuosity and silver/copper wiring determined by systemic blood pressure. Higher VEGF levels result in greater venous dilation and tortuosity. Poor ocular perfusion can mask vascular dilation and tortuosity.
Central Retinal Artery Occlusion

- Initial Va is CF to LP

- NLP without cherry-red spot, consider ophthalmic artery occlusion
  - Higher incidence of GCA
  - Approximately 5% are GCA related

- Emboli are visible in 20-40% of cases

Central Retinal Artery Occlusion (CRAO)

- Irreversible damage occurs at 90 minutes

- Possible early treatment
  - Ocular massage
  - Breathing 95% O2/ 5% CO2
  - AC paracentesis/IOP lowering
CRAO with Cilioretinal Artery Sparing

Partially perfused retina are the most dangerous CRAO - RISK OF RAPID NEOVASCULAR GLAUCOMA!!!
As early as 2 weeks!

Must monitor for development of NVD, NVE and NVI

IVFA:
- Delayed arterial filling
- Delayed A-V transit

Retinal Artery Occlusion (RAO)

- Must monitor for development of NVD, NVE and NVI
- IVFA:
  - Delayed arterial filling
  - Delayed A-V transit
Central Retinal Vein Occlusion

- 70% non-ischemic (low-risk NV)
  - Va >20/200
  - 5-20% convert to ischemic within a few months
  - 34% perfused CRVO convert over 3 years
- 30% Ischemic
  - Va ~CF, +RAPD [Probably most important finding]
  - >10 DD Non-perfusion on FA [Old criteria]. New criteria have not been defined with WAFA.
- High-risk NVA/NVI
- Low-risk NVE/NVD
CRVO Management

- Follow closely for NVI/NVA/NVG
  - Gonioscopy monthly for first 3 months
  - “90 day glaucoma”
- PRP once neovascularization develops
- CME
  - Anti-VEGF
  - Corticosteroids
- Initiate Anti-VEGF if any ME
- Debate on if Anti-VEGF indicated at venous stasis retinopathy phase

BRVO

- Arteriole compression leads to thrombus formation and leakage from capillary beds
  - 1. HRVO - Before 1st bifurcation
  - 2. Intermediate/Quadrant (most common) - After 1st bifurcation
  - 3. Twig - Macular area only
BRVO

- Non-Ischemic (70-80%):
  - Treat macular edema with Va <20/40 (old criteria)
  - Treat if any macular edema present!

- Ischemic: <20/200; 5DD nonperfusion
  - NVI/NVA rare | NYD/NVE common

- HRVO – behaves like BRVO
Non-perfusion

Dye Leakage

Anti-VEGF in RVO

- Increasing evidence from long-term study results (> 3 years) - Improvement in retinal vasculature on FA and exam
- Even if no ME or minimal ME is present, sustained anti-VEGF injections can maintain a healthier vasculature
- Chronic disease- Can treatment be a cure? Presently, treatment aimed at symptomatic relief (vision-macular edema) and complication prevention (NY/NVG).

Venous vascular caliber and tortuosity is governed by perfusion and intraocular VEGF levels and blood outflow compromise
- Arterial vascular tortuosity and silver/copper wiring determined by systemic blood pressure
- Higher VEGF levels result in greater venous dilation and tortuosity
- Poor ocular perfusion can mask vascular dilation and tortuosity

RECAP: Key Principles of Understanding VEGF Drive
Diabetic Retinopathy

- Inflammatory & Ischemic Disease Process
- Importance of IVFA (Ischemic process)
  - Macular perfusion
    - Guides therapy & Prognosis
  - Peripheral non-perfusion
    - Chronic macular edema
    - Retinal neovascularization
    - NVI/NVA/NVG
- Old Treatments: PRP and Focal Laser
- Current Treatments: PRP/Focal/Anti-VEGF
Diabetic Retinopathy

- Results in Two Causes of Vision Loss
  - Proliferative Diabetic Retinopathy-Vitreous Hemorrhage/Tractional Retinal Detachment
  - Diabetic Macular Edema
- Treatments (Old paradigm)
  - PDR- Panretinal Photocoagulation
  - DME- Focal Laser

Diabetic Retinopathy

- Treatments (New paradigm)
  - PDR
    - If Early—Anti-VEGF Therapy
    - If Significant NV — PRP Laser
  - Mild-Early PDR - Longer studies are starting to demonstrate potential reversibility of diabetic retinopathy with sustained monthly injections (after 2-3 years)
  - DME- Anti-VEGF / Steroids / Focal Laser
Extensive Capillary Drop out but Macula Still Perfused

20/20 Vision with very few clinical findings, also known as the featureless retina in some textbooks
Diabetic Retinopathy

- Widefield Angiography and anti-VEGF therapy has revolutionized our understanding and approach to nuanced aspects of DR
- We still use PRP/Focal Laser but are now able to use it in a consistent fashion to modulate VEGF levels in the retina
- The aim of laser is to ease patient burden of frequent eye visits/injections

Diabetic Retinopathy

<table>
<thead>
<tr>
<th>Study</th>
<th>No. of patients</th>
<th>Anti-VEGF agent</th>
<th>Early vision</th>
<th>Late vision</th>
<th>Follow-up period</th>
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<td>Ranibizumab</td>
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<tr>
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<tr>
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<tr>
<td>VISTAR</td>
<td>276</td>
<td>None</td>
<td>3-4 (3-5)</td>
<td>3-4 (3-5)</td>
<td>12</td>
</tr>
</tbody>
</table>

* % of patients with +1 line vision gain or loss (vs. with laser therapy alone).

- VISTA- Eylea for DME

Diabetic Retinopathy

- Protocol T
- Demonstrated superior efficacy of antiVEGF for DME in the following order: Eylea > Lucentis > Avastin
- Future laser therapy: Micropulse Laser- Is it superior?
Diabetic Retinopathy

- New diabetic studies aimed at evaluating if sustained anti-VEGF injections will reverse retinopathy changes
- Ideal world- Monthly AntiVEGF injections indefinitely
  - Poses an incredibly healthcare burden
  - Cost and Time both on patient and society
  - Care aimed at compromise of worlds

Hypertensive Retinopathy

- Retinal arteriolar damage
  - Diffuse or focal vasospasm
  - Arteriosclerosis (thickening of the vessel wall)
- Fibrinoid necrosis of the choroid
Non-Perfusion
Dye Leakage
RMA
- 75% associated with HTN
- Arise within 1st three bifurcations
- Spontaneous thrombosis of aneurysm can occur
- Typically female >60yo
- Bleeding can occur at all 3 levels of the retina

RMA Management
- Observe
- Chronic exudation
  × Anti-VEGF (less role since structural) - only beneficial if avascular VEGF drive is present promoting leakage
  × Laser
- Hemorrhage
  × YAG/hyalidotomy
  × Vitrectomy
Clinical Findings

- Nonproliferative retinal changes
  - Venous tortuosity
  - Salmon-Patch hemorrhage
  - Black Sunburst
  - Iridescent spot
- Proliferative retinal changes (SC dz)
  - NVE, vitreous hemorrhage, and tractional retinal detachments
Management

- Observation
- Photocoagulation
- Cryotherapy
Questions
Case 1- Lattice Eval

- 14 year old Vietnamese girl with congenital glaucoma and myopia, referred in for evaluation of lattice degeneration both eyes

- VA 20/20 OU
- IOP OD: 17 mmHg OS: 18mmHg
- Meds: Azopt BID both eyes
- FamHx: Negative for any eye diseases
- Soc Hx: Full-Term
Differential Diagnosis:

- Lattice Degeneration
- Peripheral Microcystoid Degeneration/Snowflake degeneration
- Anomalous Vitreous Base
- Peripheral Neovascular Changes
  - Eales Disease
  - Sickle Cell Retinopathy
  - Retinopathy of Prematurity
  - Incontinentia Pigmenti
  - Familial Exudative Vitreoretinopathy

What test to order next, if any?
Diagnosis

• Familial Exudative Vitreoretinopathy
• Mutations: FZD4, LRP5, Tspan12, NDP
• Wnt signaling pathway mutations
• Autosomal Dominant

Treatment

• Fluorescein Guided Pan-Retinal Photocoagulation to Avascular Retina
• Follow-up interval- Depends on disease activity, age, systemic health- ranging from monthly to every 6 months

Case 2- ROP vs. Tumor?

• 2 week old PMA (GA 36 weeks, 3.5 pounds) healthy African American infant noted to have eye crossing.
• VA BTL OU
• IOP soft normal tactile OU
• Meds: None
• FamHx: Negative for any eye diseases per Mom
• Soc Hx: Full-Term. Mom had Stage 4 Lymphoma during pregnancy
Differential Diagnosis:

- Retinopathy of Prematurity
- Incontinentia Pigmenti
- Sickle Cell Retinopathy
- Muscular Dystrophy Associated Neovascularization
- Norrie’s Disease
- Persistent Fetal Vasculature
- Tumor/Lymphoma
- Familial Exudative Vitreoretinopathy
What test to order next, if any?
Diagnosis

• Familial Exudative Vitreoretinopathy

Treatment

• Fluorescein Guided Pan-Retinal Photocoagulation to Avascular Retina
• Family Needs to be Screened- Mom evaluated (carrier)
• Follow-up interval- Depends on disease activity, age, systemic health- ranging from monthly to every 6 months

Family Screening

• Biological Parents need to be evaluated
• Mom was screened. Father was unable to be evaluated. Subsequent photos show mom was the carrier.
Case 3-Skin Blisters

- 6 month old Caucasian female baby (Full-term) healthy, vaginal delivery with no visual complaints.
  
  - VA F&F OU
  - IOP soft tactile OU
  - Meds: None
  - Fam Hx: Negative for any eye diseases
  - Soc Hx: Full-Term. Negative h/o maternal miscarriage
Differential Diagnosis:

- Retinopathy of Prematurity
- Familial Exudative Vitreoretinopathy
- Thalassemias
- Incontinentia Pigmenti

What test to order next, if any?
Diagnosis

- Incontinentia Pigmenti (Bloch Sulzberger Syndrome)
- X-Linked Dominant
- NEMO mutation
- Delayed Tooth Eruption / Skin Blisters
- Possible Delayed Cognitive Development
- Fatal in males / Unexplained vitreous hemorrhage in a 30-40 year female
Treatment

- Fluorescein Guided Pan-Retinal Photocoagulation to Avascular Retina
- Follow-up interval- Depends on disease activity, age, systemic health- ranging from monthly to every 6 months

Case 4-

- 18 year old seen by another retina specialist (different group) who disagreed with the optometrists referral of Best’s disease.
- VA OD: 20/40 OS: 20/200 Eccentric
- IOP OD: 14 mmHg OS: 14 mmHg
- Meds: None
- FamHx: Negative for any eye diseases
- Soc Hx: Full-Term
Differential Diagnosis:

- Cone Dystrophy
- Bulls-Eye Maculopathy from Drug Toxicity
- Methylcobalamin Deficiency
- Best Disease (Autosomal Dominant)
- Sorsby Pseudoinflammatory Dystrophy
- Age Related Macular Degeneration
- Bilateral idiopathic CNV
What test to order next, if any?

Testing

- Electrooculogram (Not Done)
- Electroretinogram (Not Done)
- Fluorescein Angiography
- Autofluorescence
- Genetic Testing (What Genes?)
Diagnosis

- Best Disease
- Autosomal Recessive (NOT Autosomal Dominant)
- Genetics Pending
- EOG confirmed with low Arden ratio
Treatment

- Anti-VEGF Therapy for CNV
- Observation/Amsler Monitoring
- Potential future gene therapy / Challenge is the size of the bestrophin gene

Case 5-

- 12 year old African American girl with referred in with history of sickle cell disease in family. No vision complaints.
- VA 20/20 OU
- IOP OD: 12 mmHg OS: 12 mmHg
- Meds: None
- Fam Hx: Negative for any eye diseases
- Soc Hx: Full-Term
Differential Diagnosis:

- Fairly Normal Looking Fundus
- Denies any sickle crisis
- What questions to ask in a family history of sickle cell?
- What test to order, if any?
Diagnosis

- HgbSC Retinopathy

Treatment

- Fluorescein Guided Pan-Retinal Photocoagulation to Avascular Retina
- Follow-up interval- Depends on disease activity, age, systemic health- ranging from monthly to every 6 months
Conclusion

- Careful Review of Systems
- Systemic Associations
- Family History
- Knowledge of various disease entities present to narrow differential
- Vigilance not only about clinical/exam correlation but also simply history- Know when to send out for referral
- Early disease presentation often has no or minimal exam findings!

Staged Limbal Based Vitrectomy for Closed Fun

Cutis Marmorata Congenita Telangiectata
AMD Puckers and Holes - You can surgically do what to the macula?

Emmanuel Chang, MD PhD
Adult and Pediatric Vitreoretinal Diseases and Surgery
Retina and Vitreous of Texas

Macular Holes

• 1st described in 1869 by Dr. Knapp due to trauma
• 92% of macular holes is idiopathic
• Average age 68
• Female > Male
• Approximately 1.5% of population have vitreomacular traction related disorders

Etiologies

• Idiopathic
• Myopia
• Traumatic
• Chronic CME
• Post Macular Off Retinal Detachment Surgery
• Laser/Lightning
• Epiretinal Membranes
Stage 0
- Normal Vitreomacular interface
- Stage 0 Vitreomacular adhesion

Stage 1 OCT Findings

Stage 2
- Full thickness defect without hyaloidal separation

Stage 3
- Full thickness defect with separation of the hyaloid from the macula

Stage 4
- A Stage 3 Hole with a Complete PVD
Macular Hole Mimickers

- ERM with Pseudohole

S/P Surgical Repair

ICG-Assisted ILM Peeling

Foveal ILM is ONLY 400 nanometers thick!

Hair is about 100 microns thick - ILM is 0.4 microns!
So, what? You can peel the surface of the retina, what can you do under the retina?

Removal of Subretinal Scar due to Choroidal Neovascular Membrane in AMD/PPCNV

Well, what if you can’t see under the retina to remove the sub retinal CNV because there is a massive sub retinal bleed?
Okay. So, you can clear sub retinal blood and remove sub retinal CNV. But, what if the tissue is already dead. You have a subfoveal geographic atrophy or scar?
Conclusion

- There are many surgical tools available to the well-trained vitreoretinal surgeon
  - Peeling submicron retinal tissue layers
  - Removing subretinal vascular membranes
  - Displacing subretinal/submacular bleeds
  - Rotation of retinal tissue
- Many more tools to come in the future such as stem cell transplantation and retinal prosthetic implants
The Future of AMD
What do I need to know on the horizon?

Emmanuel Chang, MD PhD
Retina and Vitreous of Texas
Vitreoretinal Diseases and Surgery

Disease Framework

- Dry (non-neovascular) Age Related Macular Degeneration
- Wet (neovascular) Age Related Macular Degeneration

Masqueraders
- Pattern Dystrophy
- Age Related Choroidal Atrophy
- Polypoidal Choroidal Vasculopathy

Current Clinical Paradigm
Dry (non-neovascular) Age Related Macular Degeneration

- Amsler Grid Monitoring
- AREDS/AREDS2 Eye vitamins for Category 2 or higher
- No real role for AREDS vitamins once Category 4-Wet AMD
- Macular translocation surgery
Dry AMD

AREDS - Category Classification

- Category 1: No AMD. A few small drusen.
- Category 2: Mild AMD. Several small or one medium drusen.
- Category 3: Moderate AMD. Many medium or one large drusen.
- Category 4: Advanced AMD. Any RPE atrophy or CNV.

Avoid Beta-Carotene if smoker within the last 15 years

Dry AMD - 2013

AREDS2 Formulation - 25% risk reduction Cat 4

- Consists of previous AREDS
  - 500 mg Vit C / 400 IU Vit E
  - 80 mg Zinc / 2 mg Copper
  - + 10 mg Lutein
  - + 2 mg Zeaxanthin
- Omega-3/Fish Oil did not show to have a benefit in reducing risk of progression
- Study showed that removing beta-carotene and lowering zinc did not have an effect on progression. Since at least 50% of AMD patients are smokers or former smokers, the decision from a lung cancer benefit for removal of beta-carotene was elected.

Dry AMD

The Problem is We Don’t Understand the Basic Pathophysiology of Disease!!!
Dry AMD - Five Areas of Targets / Future Paradigm

- Nutrient supplementation - AREDS/AREDS2
- Visual Cycle Modulation - Fenretinide & Acucela
- Neuroprotection
- Complement Inhibition - Lampalizumab
- Stem Cell Therapy

Dry AMD - Visual Cycle Modulation

*Fenretinide*

- Synthetic Vitamin A Homologue
  - Does not interconvert with Vitamin A
  - Fenretinide competes with vitamin A for binding to retinol binding protein (RBP) and does not allow transthyretin to bind to the complex.
  - This RBP complex with fenretinide is then secreted through the kidneys.
  - Did show 300 mg of fenretinide showed growth of geographic atrophy slowed by 40% at 18 months.
Dry AMD - Visual Cycle Modulation

*Acucela*

- Emixustat Hydrochloride / ACU-4429
- Visual Cycle Modulator
- Slows Vit A Accumulation Toxins
- Reduces Oxidative Stress
- It is a non-retinoid molecule that inhibits RPE65 which reduces rate of Vit A processing in the visual cycle, thereby slowing production of lipofuscin A2E

Dry AMD - Five Areas of Targets / Future Paradigm

- Nutrient supplementation - AREDS/AREDS2
- Visual Cycle Modulation- Fenretinide & Acucela
- Neuroprotection
  - Complement Inhibition- Lampalizumab
  - Stem Cell Therapy

Dry AMD - Neuroprotection

- Neurotech CNTF Secreting Implant
- Brimonidine
- OT-551 Oxidative Stress Inhibitor

- All have not shown to be beneficial in slowing down the disease
Dry AMD - Five Areas of Targets / Future Paradigm

- Nutrient supplementation - AREDS/AREDS2
- Visual Cycle Modulation - Fenretinide & Acucela
- Neuroprotection
- Complement Inhibition - Lampalizumab
- Stem Cell Therapy

Dry AMD - Complement Inhibition Lampalizumab

- Complement Factor D Inhibition Antibody
- MAHALO Clinical Trial
  - At 18 months, geographic atrophy size was reduced by 20%
  - Rate of progression was reduced by 44% in certain patient groups
  - Introduces concept that genetic profiling of AMD/Complement mutations may have select targeted therapeutics such as Factor D inhibition
Dry AMD - 2015

- Stem Cell Therapy - Human Pluripotent Stem Cells
  - 2 Sources
    - Human Embryonic Stem Cells (hESCs)
      - From inner cell mass of day-5 human blastocysts leftover from in vitro fertilizations
    - Human Induced Pluripotent Stem Cells (hiPSCs)
      - Reprogrammed somatic cells
      - Umbilical Cord Cells

Dry AMD - Stem Cell Therapy

Dry AMD - 2015

- Stem Cell Therapy
  - Preliminary Promise in Preserving/Restoring RPE Cells
  - Controversial - Initial Studies showed many of the cells did not survive. Ongoing studies are transplanting even larger number of RPE Stem Cells
  - Need to be on lifetime immunosuppressive therapy
  - This is a cell transplant!
Wet AMD

Current Clinical Paradigm
*Wet (neovascular) Age Related Macular Degeneration*
- Anti-VEGF Injections
  - Avastin/Bevacizumab
  - Lucentis/Ranibizumab
  - Eylea/Aflibercept
- Photodynamic Therapy/Verteporfin
- Subretinal CNV Surgery/Submacular heme displacement
- Macular Translocation Surgery

Wet AMD - 2015
- Anti-VEGF Inhibition
  - Avastin is a standard IgG antibody
  - Lucentis contains only the Fab fragment
  - Eylea is an engineered antibody
Wet AMD - 2015

- Anti-VEGF Inhibition
- CATT Trial - Compared Avastin against Lucentis and showed equal efficacy
  - Results: At two years, Lucentis showed only 1.4 letters better vision than Avastin under monthly treatment. 60% of patients were able to maintain 20/40 or better vision.
  - Monthly Dosing Better than PRN Dosing
    - Did NOT Evaluate Treat and Extend dosing
  - Smaller studies suggest Eylea may work better in select cases with pigment epithelial detachments

Wet AMD - Anti VEGF Risks

- CATT Subanalysis - Suggests accelerated geographic atrophy if VEGF over suppressed
  - Systemic reduction in VEGF levels / Increased risk of thromboembolic events / strokes
  - Lucentis yields lowest systemic effects on serum VEGF levels and least blood plasma level penetration because of lack of Fc portion - ? Safer Profile ?
- Risks during pregnancy

Wet AMD - 2015

- Photodynamic Therapy- Verteporfin
  - Standard treatment for Wet AMD in the 1990s
  - Verteporfin is a porphyrin molecule that generates radicals upon UV/Near IR wavelength exposure.
  - It binds to LDL receptor molecules of vessels and the oxidative stress from free radical formation causing vaso-occlusion
Wet AMD - Verteporfin

Still has a role, in particular with polypoidal variant presentations of wet AMD

Since this is a photo reactive occlusive process, may be beneficial still in achieving longer durations of action of drug effect in conjunction with anti-VEGF injections

Full Dose much less frequently done. Many do half dose.

Wet AMD - Surgical Approaches

Subretinal CNV Surgery

Submacular Heme Displacement Surgery

Macular Translocation Surgery
Wet AMD - Future Paradigms

- Targeted Brachytherapy
- Longer Acting/Increase Anti-VEGF Potency Drugs
- Sustained Release Drug Systems
- Encapsulated Cell Technology-Protein Secretion
- Anti-PDGF Drugs
- Gene Therapy/Viral Transfection of Anti-VEGF protein secretion

Wet AMD - Targeted Brachytherapy

- Epimacular Brachytherapy (Neovista)
- Intraocular strontium-90 applicator

Wet AMD - Future Paradigms

- Targeted Brachytherapy
- Longer Acting/Increase Anti-VEGF Potency Drugs
- Sustained Release Drug Systems
- Encapsulated Cell Technology-Protein Secretion
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Wet AMD - Future Paradigms

- Targeted Brachytherapy
- **Longer Acting/Increase Anti-VEGF Potency Drugs**
- Sustained Release Drug Systems
- Encapsulated Cell Technology-Protein Secretion
- Anti-PDGF Drugs
- Gene Therapy/Viral Transfection of AntiVEGF protein secretion

Wet AMD - Longer Acting Anti-VEGF drugs

- **Alcon Antibody**
  - Even stronger affinity than Eylea / Lucentis (Approximately 10 fold increased)
  - Phase 2 data showed promising results
  - Very small percentage showed potential antibody formation
  - Clinical trial design to test 3 month dosing interval after initial monthly dosing
Wet AMD - Sustained Drug Delivery

- Collagen Gel Matrix Drug Delivery of Antibodies
- PLGA Matrix Biodegradable Implant/Release of DARPin- Allergan Phase 3 Clinical Trials

Wet AMD - Sustained Drug Delivery

- Surgical implantable reservoir device- Forsight Vision4 (Licensed to Genentech- in development)

Wet AMD - Future Paradigms

- Targeted Brachytherapy
- Longer Acting/Increase Anti-VEGF Potency Drugs
- Sustained Release Drug Systems
- Encapsulated Cell Technology-Protein Secretion
- Anti-PDGF Drugs
- Gene Therapy/Viral Transfection of AntiVEGF protein secretion
Wet AMD - Encapsulated Cell Technology

- Neurotech Encapsulated Cell Technology to secrete anti-VEGF proteins
- Platform is clinically tested and approved previously with CNTF

Wet AMD - Future Paradigms

- Targeted Brachytherapy
- Longer Acting/Increase Anti-VEGF Potency Drugs
- Sustained Release Drug Systems
- Encapsulated Cell Technology-Protein Secretion
- Anti-PDGF Drugs
- Gene Therapy/Viral Transfection of Anti-VEGF protein secretion

Wet AMD - Anti-PDGF

- Most promising and fastest to market. Already in Phase 3 Trials- Fovista by Ophthotech
Wet AMD - Future Paradigms

- Targeted Brachytherapy
- Longer Acting/Increase Anti-VEGF Potency Drugs
- Sustained Release Drug Systems
- Encapsulated Cell Technology-Protein Secretion
- Anti-PDGF Drugs
- Gene Therapy/Viral Transfection of Anti-VEGF protein secretion

Wet AMD - Gene Therapy

- Viral transfection using AAV Adenovirus
- Release of sFlt protein which is a VEGF receptor ligand
- Preliminary data suggests duration of efficacy approximately 1 year

Conclusion

- Numerous exciting concepts for both Dry and Wet Age Related Macular Degeneration are on the horizon
- AMD is a complex disease that does not have a one treatment fits all and as the underlying pathophysiology of AMD is better understood, more precise personalized medical therapy can be designed for each patient.
- Genetic profiling may become a future important role similar to how gene profiling is crucial now in the use of anti-cancer drug selection in patients.
Course Description: This course examines the diagnosis and management of patients with primary and secondary glaucomas through a case based approach.

Abstract: Glaucoma diagnosis involves examination of the optic disc, visual field, and various risk factors. In a case-based format, these issues are addressed through the examination of real-life patient information to solidify understanding of glaucoma diagnosis and management.

Learning Objectives: At the end of this course, the audience will be able to:
1. Correctly diagnose and manage patients with open angle glaucoma and ocular hypertension.
2. Correctly identify mechanisms of angle closure glaucoma.
3. Correctly identify various types of secondary glaucoma.

Dear Colleagues:
This course is designed to bring you the latest information regarding diagnosis and management of patients with glaucoma. I have included in this handout some key points regarding these clinical entities; however we vastly prefer to have an engaging dialogue with the audience – this cannot unfortunately be encapsulated in a handout. Please realize that these “notes” are neither exhaustive nor organized consistent with the presentation. They simply represent some facts about the entities which we may or may not cover.

I hope you understand our philosophy and enjoy the program!

The Glaucoma Continuum: Undetectable (Normal/ Ocular Hypertension)
• Initiation of apoptosis
• Ganglion cell Death and loss of axons
• RNFL change

The Glaucoma Continuum: Detectable (Glaucoma)
• RNFL change
• Optic disc change
• Visual field changes-mild to moderate

The Glaucoma Continuum: Detectable (Blindness)
• Visual field changes- severe
• Functional visual impairment

Ocular Hypertension (OHTN)
• Ocular hypertension is defined as IOP of 21 mm hg or more in the absence of structural and functional changes
• The Myth of 16 and 21
• The Ocular Hypertension Treatment Study (OHTS) has shown that approximately 10% of patients with ocular hypertension convert to true glaucoma over the course of 5 years
• There are far more patients with OHTN than glaucoma
• Prevalence increases with age
  • 75% of ocular hypertensives are over 60 yrs.
  • 24% of people over 70 yrs may be ocular hypertensives

Epidemiology of Glaucoma
• 0.41-0.86% of Americans over 40 years have glaucoma (1-3 million Americans)
• 1 million undetected
• 95,000/yr lose sight
• #2 cause of blindness
• #1 cause in non-whites
• Approximately 4% of glaucoma patients become blind
  • However, not everyone with glaucoma has a 4% risk of becoming blind – some may be much higher or lower
• Prevalence of ocular hypertension is always greater than glaucoma
• Prevalence of glaucoma increases with age

Primary Open Angle Glaucoma (POAG)
• Most prevalent type of glaucoma
• Idiopathic
• Poor outflow of aqueous
• Typically elevated IOP (decreased outflow, not increased inflow)
  • Level of IOP is inconsistent with health of optic nerve in that individual
  • Ability to tolerate a certain level of IOP varies between patients and within the same patients as they age
• Characteristic glaucomatous neuropathy
- Rim notching
- NFL defects
- Characteristic visual field loss
- Angles open by gonioscopy
- No secondary cause: this must be established before POAG can be diagnosed. There still are cases where there is a secondary cause that has not correctly been identified.

**Histopathology of Glaucoma**
- **Anterior Segment**
  - Accelerated and exaggerated normal aging changes in anterior chamber angle.
  - Affects both Schlemm’s canal and uveoscleral outflow pathways.
  - In that POAG is largely an outflow problem, it can be said that increased resistance to outflow at the level of the juxtacanalicular tissues in the trabecular meshwork is the site of glaucoma.
- **Posterior Segment**
  - Early Changes
    1) Compression of laminar sheets
    2) Distortion of laminar pores
    3) Blockage of axonal transport
      a. IOP induced (?)
      b. Vascularly induced (?)
    4) Death of ganglion cells
    5) Deepening and enlargement of optic cup
  - Later Changes
    1) Additional compression of laminar sheet
    2) Posterior and lateral displacement of laminar sheet

**POAG: Diagnosis**
- ONH and nerve fiber layer damage consistent with glaucoma
- Visual field loss consistent with glaucoma
- Progression consistent with glaucoma
- IOP inconsistent with optic nerve health
- No other apparent or identifiable causes
- Other risk factors
  - Age, race, family history, corneal thickness, poor ocular perfusion

**POAG: Visual Field Defects**
- Increased short term fluctuation
- Small, shallow, fluctuating scotoma
- Nasal step
- Arcuate depressions
- Sensitivity depression
- Paracentral scotomas
- Superior-inferior asymmetry
- 90-93% of all field loss in glaucoma occurs within the central 30 degrees
Visual field defects are reflected by damage to the optic disc and nerve fiber layer

**Risk Factors for Developing POAG:**

- Elevated IOP: This is the most significant risk factor *overall*
  - Mean IOP 16 +/- 2.5 mm hg
  - IOP which is statistically abnormal is not necessarily physiologically abnormal for an individual eye. Conversely, IOP that is statistically normal is not necessarily physiologically normal for an individual eye. Thus, there is no clinically useful level of IOP to differentiate all normals from all people with glaucoma
  - Patients with advanced glaucoma may not be able to tolerate even moderate levels of IOP
  - Ocular hypertension is a risk factor for glaucoma, not a prerequisite
    - The level of IOP which causes damage to an optic nerve varies significantly between individuals and even in the same person as she/he ages
  - 1/3-1/2 of all glaucoma patients shows IOP below 21 mm hg on a single visit. If you do nothing other than measure IOP for the detection of glaucoma, you will miss 1/3-1/2 of the glaucoma cases in your office. IOP measurement is an inadequate screening item.
  - IOP increases with age
  - IOP decreases with exercise (transiently)
  - Increased blood osmolarity decreases IOP (mannitol, glycerin, alcohol)

- **Diurnal Variation of IOP**
  - < 5 mm is normal
  - Glaucoma patients: 15 mm or more can occur, especially with secondary glaucomas
  - It was once thought that IOP peaked in the morning and decreased throughout the day. It was also thought that IOP dropped during sleep due to aqueous production suppression; however, we have recently learned that the highest IOP occurs when the patient is sleeping in the supine position.

- **Age**
  - Older disease

- **Race (1/8 blacks over age 60 develop glaucoma)**
  - Earlier onset
  - More aggressive course
    - Especially aggressive in patients of Caribbean descent
  - Older Hispanics have higher incidence of glaucoma than pts of African descent

- **Family History**
  - Direct relative- parent, sibling, child
  - History of blindness very important

- **Central Corneal Thickness (CCT)**
  - Thick corneas overestimate true applanation pressure and thin corneas underestimate true applanation pressure. However, beyond errors imparted by applanation, patients with thin corneas have greater risk of converting to glaucoma from ocular hypertension, are more likely to progress in glaucomatous
damage, and are more likely to have structural and functional changes.

- Possibly indicative of other structural weaknesses within the eye predisposing to glaucoma, but this is only speculative and not proven
- Don’t know if thin cornea in normal populations is risk factor alone, thus checking corneal thickness on every patient is not indicated
- Thin cornea is a risk factor for glaucoma at all levels of IOP, thus independent of IOP
- There is no scientifically validated conversion factor to adjust for the role of CCT on IOP.

- Diabetes
  - Controversial- likely a minimal impact/ risk factor
- Hypertension (HTN)
  - Causing vascular compromise and arteriolosclerosis
    - Treatment of HTN may actually contribute to ONH damage
- Hypotension, carotid artery disease, cardiac disease
  - Causing poor ONH perfusion
- Ocular Perfusion Pressure (OPP)
  - The difference between systemic blood pressure and intraocular pressure.
    - A measure of retinal and optic nerve perfusion
- Systolic Perfusion Pressure (SPP)
  - SPP = Systolic Blood Pressure – IOP
- Diastolic Perfusion Pressure (DPP)
  - DPP = Diastolic Blood Pressure – IOP
- Mean Perfusion Pressure (MPP)
  - MPP = Mean arterial pressure – IOP
    - Mean Arterial Pressure = 2/3 DBP + 1/3 SBP
- Baltimore Eye Survey
  - Lower OPP strongly associated with prevalence of POAG
  - Six-fold excess risk of having glaucomatous optic nerve damage in persons with lowest category of OPP
- The Egna-Neumarkt Study
  - Lower DPP associated with a higher risk of having glaucomatous optic nerve damage
- Proyecto Ver Study
  - Persons with Diastolic Perfusion Pressure < 50 mmHg had a four-fold higher risk of having POAG compared to those with Diastolic Perfusion Pressure of 80 mmHg
- Los Angeles Latino Eye Study
  - Persons with Low Diastolic and Systolic perfusion pressures had a higher risk of having POAG
- Barbados Incidence Study
  - 4-year risk of developing glaucomatous optic nerve damage increased dramatically at lower
    - Systolic Perfusion Pressure  2.6 fold
    - Diastolic Perfusion Pressure  3.2 fold
• Mean Perfusion Pressure 3.1 fold
• 9-year risk of developing glaucomatous optic nerve damage increased at lower
  • Systolic Perfusion Pressure 2.0 fold
  • Diastolic Perfusion Pressure 2.1 fold
  • Mean Perfusion Pressure 2.6 fold
• Glaucoma medications can affect OPP
  • Prostaglandin analogs and carbonic anhydrase inhibitors increase DPP at all time points
  • Beta blockers decrease DPP from 4 am – 4 pm but not at other times
  • Alpha agonists reduce DPP at multiple time points

Sleep Apnea:
• Glaucoma prevalence in pts with obstructive sleep apnea (OSA) 5.7 – 27%
• OSA prevalence in glaucoma 20-55%
• However, 5 recent studies saw no association between glaucoma and OSA
  o Still an unknown entity in glaucoma risk factors

Cerebrospinal Fluid Pressure (CSF)
• Studies have shown that the anatomy of the optic nerve head including the intraocular pressure, the anatomy and biomechanics of the lamina cribrosa and peripapillary sclera, retrobulbar orbital cerebrospinal fluid pressure and the retrobulbar optic nerve tissue pressure may be of importance for the pathogenesis of open angle glaucoma
• An experimental investigation suggested that a low cerebrospinal fluid pressure may play a role in the pathogenesis of normal (intraocular-) pressure glaucoma
• Recent clinical studies reported that patients with normal (intraocular-) pressure glaucoma had significantly lower cerebrospinal fluid pressure and a higher trans lamina cribrosa pressure difference when compared to normal subjects. One may, therefore, postulate that a low cerebrospinal fluid pressure may be associated with normal (intraocular-) pressure glaucoma. A low systemic blood pressure, particularly at night, could physiologically be associated with a low cerebrospinal fluid pressure, which leads to an abnormally high trans lamina cribrosa pressure difference and as such to a similar situation as if the cerebrospinal fluid pressure is normal and the intraocular pressure is elevated.

Glaucomatocyclitic Crisis
• AKA Posnner-Schlossman Syndrome
• Ocular hypertensive syndrome associated with mild anterior chamber reaction
• Occurs mostly between ages of 20 and 60 years, and is rare over age 60
• Unilateral
• Recurrent
• Intervals of months to years
• Mild symptoms, or may be asymptomatic
• Blurred vision secondary to corneal edema common
• Mild anterior chamber reaction
• Keratic precipitates are often the only sign of inflammation, and may not even be present
  • Flat, round, and non-pigmented
  • Concentrated over inferior endothelium
• The conjunctiva may be white and quiet, or mildly injected
• Anterior chamber angle is open and normally pigmented
• Pupil may be mid-dilated
• Iris hypochromia may occur, but is uncommon
• High IOP (30 mm Hg-60 mm Hg is typical, but 90 mm Hg has occurred)
• IOP elevation can precede inflammation signs
• IOP level is disproportional to amount of inflammation
• Self limiting
• Duration: hours to weeks- typically will last for several days, but can persist for months
• Normal fields and discs (?)
  • There is a strong association with POAG in these patients
  • All findings normal between attacks (?)

Glaucomatocyclitic Crisis: Pathophysiology
• An obscure etiology.
• Decreased outflow suggests a trabeculitis as the causative mechanism.
• Prostaglandin E (causing a breakdown of the blood-aqueous barrier) found in high concentrations, which may increase the blood-aqueous barrier permeability and lead to increased aqueous production.
• Also, prostaglandins will lead to an increase in cells and proteins in the AC due to the barrier breakdown.
• Prostaglandin E has been found in high levels during acute attacks and normal levels have been found in the same patients during normal times.
• Prostaglandin inhibitor indomethacin has been more effective at lowering IOP than diamox, dexamethasone, and epinephrine

Glaucomatocyclitic Crisis: Treatment
• This is self-limiting and will spontaneously resolve. If you are sure of the diagnosis, the patient can potentially be monitored without medical treatment. If you decide to treat (and it is recommended that you do treat), direct treatment toward the inflammation first and the ocular hypertension secondarily. Avoid miotics and prostaglandin analogs. Cease treatment between attacks, and monitor closely between attacks as there is a high incidence of concomitant POAG in these patients. These patients may develop POAG or they may spend more time in attacks than normal and this will lead to permanent damage.
• Corticosteroids are treatment of choice
• Cycloplegics/mydriatics are generally unnecessary
• Beta blockers, alpha adrenergic agonists, CAI’s

Primary Angle Closure With Pupil Block
- Irido-lenticular apposition
- Mid dilated state causes most problems
- Absent egress of aqueous to anterior chamber
- Pressure buildup
- Iris bombé: bowing forward of iris due to posterior pressure buildup.
- Irido-corneal apposition
- Closure of angle
- Permanent synechial closure if contact remains too long
- Alleviated by dilation or miosis (?): Miosis has long been the standard to pull the iris out of the angle, but anything that alleviates the irido-lenticular apposition will benefit.
- Very few doctors will dilate a patient in angle closure
- IOP rise (40-70 mm Hg or higher)
- Possible central retinal artery closure due to elevated IOP
- Peripheral anterior synechiae (PAS) formation
  - Permanent
- Laser Peripheral Iridotomy (LPI) or trabeculectomy: LPI reestablishes communication between the anterior and posterior chamber, thus relieving posterior pressure and allows the iris bombé to relax and the angle to ultimately open and is most appropriate treatment.
- Potentially curable
- Prevalence: 0.09%
- Anatomic features:
  - Small corneal diameter
  - Thick lens
  - Small axial length
  - Moderate hyperopia
  - Shallow anterior chamber

**Angle Closure Glaucoma: Chronic**
- Most difficult to Dx
- Asymptomatic
- PAS - zippering shut of angle
- Especially superior angle
- Discovered on routine exam
- Cataract and glaukomofleken
- Mistaken for POAG - do gonioscopy
  - value of indentation gonioscopy
- Iridotomy first, then filtering surgery if not controlled

**Angle Recession**
- Cleavage of ciliary body muscles
- Widening and deepening of angle
- Fellow eye comparison is necessary because this is not obvious
• Problems occur years after antecedent trauma
• This should be your first thought when encountering unilateral glaucoma
• Etiology is thought to be trabecular meshwork scarring/sclerosis
• 10-20% angle recession pts. develop secondary glaucoma
• Severity of glaucoma related to extent of recession

**Angle Recession Management**

• Observation if IOP, discs normal
• Fair to poor response to medication
• Aqueous suppressants
• Miotics very questionable due to changes in meshwork
• Prostaglandin analogs seem to work well- probably the best
• Beta blockers, CAI's
• Argon laser trabeculoplasty very questionable - poor response if recession > 180°
• Filters work well
• POAG more common in fellow, uninjured eye. These patients may have predisposition to glaucoma

**Lens Induced Glaucoma: Phacolytic**

• Elevated IOP in association with hypermature cataract
• Acute onset of pain and redness in an eye that is non-seeing
• Vision typically is in light perception range
• IOP typically exceeds 35 mm Hg
• Hypermature cataract - lens leaks out internal proteins, which are antigenic. Capsule ruptures and extrudes lens proteins into anterior chamber
• Antigen/antibody reaction and subsequent A/C reaction
• Provokes macrophage response
• Heavy molecular weight proteins become soluble
• Proteins can leak out through an intact capsule
• Liquefaction of lens cortex and attenuation of lens capsule
• White flocculent material in chamber and on lens surface
• Bloated macrophages with lens material within them found in anterior chamber
• PMN’s, plasma cells, and lymphocytes are typically absent
• Variable anterior chamber reaction, heavy flare typical, hypopyon and KP’s rare
• Outflow blockage
• Trabecular meshwork effects (open angle)
• If inflammation is bad enough, there can be posterior synechiae and pupil block with angle closure or angle closure without pupil block.
• Cured by lensectomy and vitrectomy
  • Some surgeons have had success with ECCE without vitrectomy
  • Possibility of capsular rupture with vitrectomy required
  • ICCE often the procedure of choice
• Medical therapy initially to temporize IOP and quell inflammation
  • Corticosteroids Q15min to Q2H, depending upon severity
- Cycloplegia (unless there is zonular damage and danger of subluxation):
  homatropine 5%, scopolamine ¼%, atropine 1%
- Beta blockers, alpha adrenergic agonists, CAI’s
- Avoid Xalatan
- Avoid miotics at all costs!

Ocular Hypertension Treatment Study (OHTS)
- Notable feature: OHTS is the first and only NEI funded ophthalmologic study that uses an optometrist as a principal investigator (G. Richard Bennett, O.D.)
- The Ocular Hypertension Treatment Study (OHTS) is a long-term, randomized, controlled multicenter clinical trial. Ocular hypertensive subjects judged to be at moderate risk of developing primary open-angle glaucoma are randomly assigned to either close observation only or a stepped medical regimen. Medical treatment consists of all commercially available topical antiglaucoma agents. 1636 patients
- In univariate analyses, baseline factors that predicted the development of primary open-angle glaucoma (POAG) included older age, race (African American), sex (male), larger vertical cup-disc ratio, larger horizontal cup-disc ratio, higher intraocular pressure, greater Humphrey visual field pattern standard deviation, heart disease, and thinner central corneal measurement. In multivariate analyses, baseline factors that predicted POAG included older age, larger vertical or horizontal cup-disc ratio, higher intraocular pressure, greater pattern standard deviation, and thinner central corneal measurement.
- Notably, the study concluded that that lowering IOP in patients with ocular hypertension reduced the risk of developing glaucoma in five years from 9.5% to 4.4%. Thus, IOP reduction in ocular hypertension did benefit some patients. However, it is also easy to see that initiating therapy on every patient with ocular hypertension would result in gross over-treatment.
- Topical ocular hypotensive medication was effective in delaying or preventing onset of POAG in individuals with elevated IOP. Although this does not imply that all patients with borderline or elevated IOP should receive medication, clinicians should consider initiating treatment for individuals with ocular hypertension who are at moderate or high risk for developing POAG.
- OHTS also attempted to identify which patients would most likely benefit from treatment. There were some surprising results. While race (blacks) and family history were expected to be predictive of the development of POAG, they weren’t strongly predictive. Surprisingly, the presence of diabetes seemed to protect patients from the development of glaucoma. Not unexpectedly, older age, larger initial cup-to-disc ratio, and higher IOP were predictive of glaucoma.
- However, the factor that was most predictive was the presence of a thin central cornea. Patients with a central corneal thickness of 555 μm or less had a three-fold greater risk of developing POAG than those with a central corneal thickness of 588 μm or greater. The theory holds that the rigidity of a thick cornea artificially elevates the Goldmann applanation measurement of IOP and a thin cornea consequently lowers the reading of the true IOP, though other unknown factors may contribute to this finding.
• Central corneal thickness appears to be a powerful predictor of the progression from ocular hypertension to POAG. The study shows patients with thin central corneas are likely to benefit most from IOP reduction. Rarely are the conclusions of a landmark study so emphatic: At this time, measurement of central corneal thickness is necessary to accurately manage patients with ocular hypertension.

• Studies looking at glaucoma development or progression need study endpoints. Typically, study endpoints are progression of visual field damage or progressive damage to the optic disc. The vast majority of patients in glaucoma studies reach the study endpoint with progressive damage to the visual field. Very few patients reach a study endpoint by demonstrating progressive damage to the optic disc. The OHTS study was unique in that the majority of patients reached the study endpoint by having progressive damage to the optic disc rather than progressive damage to the visual field.

• Currently, OHTS II is underway. Essentially, the original patients will be followed until death. Additional features include genetic analysis and serologic studies. Because of the risk of progression to glaucoma seen at 7-8 years, all patients are now being treated. One goal is to see if there is any difference between those patients treated early compared to those treated at the end of OHTS.
Dear Colleagues:

This course is designed to bring you the latest information regarding management of retinal and uveal conditions. I have included in this handout some key points regarding these clinical entities to satisfy the course requirements, however I vastly prefer to have an engaging dialogue with the audience – this cannot unfortunately be encapsulated in a handout. Please realize that these “notes” are neither exhaustive nor organized consistent with our presentation. They simply represent some facts about the entities which I may or may not cover. I hope you understand my philosophy and enjoy the program!

Diagnoses – in Alphabetical Order:

**Diagnosis: Benign episodic pupillary mydriasis**

**Signs and Symptoms:**
- Episodic unilateral mydriasis
  - Lasts minutes to weeks
- Accompanied by blurred vision and headache
- Young healthy females predominate
- Peculiar sensations about affected eye
  - Often progresses to headache
  - Not typical migraine
- Defective accommodation
- Lid and motility defects not present
- Extensive medical testing unremarkable
Pathophysiology:
- Increased sympathetic activity?
  - Reverse Horner’s syndrome? Not likely
- Pupil paralysis following migraine?
  - Tends to last longer – not likely
  - No ophthalmoplegia
- Segmental spasm of iris dilator muscle?
  - Pupil round, so not likely
- Pharmacologically dilated?
  - Parasympatholytic – no reactivity whatsoever
  - Sympatholytic – can mimic and must be ruled out
- Anisocoria greater in bright light than dim
  - Parasympathetic dysfunction
    - Not an aneurysm
    - Edinger-Westphall lesion?
- Migraine variant – most likely etiology
- Treatment – none except to avoid unnecessary testing

**Diagnosis: Carotid cavernous sinus fistula**

**Cavernous sinus anatomy**
- CN III, IV, V1, VI, oculosympathetics, internal carotid artery
- Superior and inferior ophthalmic vein drains eye and adnexa to sinus and out via inferior and superior petrosal sinus to jugular vein

**Fistula:**
- Rupture of intracavernous portion of internal carotid artery (ICA) or meningeal branch
  - Meningohypophyseal, McConnell’s Capsular, or Inferior Cavernous artery
- Mixing of high pressure oxygenated blood into low pressure deoxygenated venous system

**Fistulas: Classification**
- Hemodynamically
  - High flow (ICA rupture) or low flow (meningeal branch)
- Angiographically
  - ICA or meningeal branches ruptured
- Etiology
  - Traumatic (ICA rupture) or spontaneous (meningeal branch)
    - Theorized that there are small aneurysms on meningeal branches in hypertensive, middle age females which rupture and lead to low flow fistula

**Carotid Cavernous Sinus Fistula: Signs and Symptoms**
- Increased venous pressure
- Orbital congestion
- Proptosis (pulsatile)
- Corneal exposure
- Arteriolization of conjunctival and episcleral vessels
  - “Caput Medusa”
    - Medusa’s head of snakes
- Orbital bruit
- Myopathies and cranial neuropathies with diplopia and ophthalmoplegia
- Secondary glaucoma from increased episcleral venous pressure
  - High-pressure arterial blood increases pressure in venous system.
  - Blood backs up and moves toward eye through superior ophthalmic vein
  - Episcleral veins increase pressure
    - IOP always exceed episcleral venous pressure

**Carotid Cavernous Sinus Fistula: Management**
- Vision threatening – not life threatening
- Spontaneous etiology – spontaneous resolution
  - Wait it out for a few months – monitoring is most prudent
- Traumatic
  - Clipping and ligation
  - Balloon or particulate embolization
- Glaucoma difficult to manage
  - Prostaglandin analogs most suited because they decrease IOP independent of episcleral venous pressure

**CN III Anatomy:**
- CN III is the only CN with a sub-nuclear complex
  - Medial rectus (MR), inferior rectus (IR), superior rectus (SR-decussates with contralateral innervation), inferior oblique (IO), levator (bilateral upper lid)
- Paired sub-nuclei with decussation of one sub-nuclei
- One unpaired sub-nuclei controls both eyelids
- Arises in the midbrain (mesencephalon) at the level of the superior colliculus
- Breaks into a superior and inferior division
- Pupillomotor fibers travel with the inferior division and the inferior oblique

**CN III Palsy: Clinical Picture**
- Eye that is down and out with a ptosis
- Pupil features
  - Pupil may be dilated (involved) or normal (spared)
- Variations
  - Palsy is complete; paresis is incomplete
- Signature motility of CN III palsy:
  - A hyper deviation that increases in up gaze, reverses in down gaze
  - Exo deviation which increases in opposite gaze
- Other possibilities
• Remember the possibility of a partial paresis or isolated muscle paresis. Isolated muscle paresis are in the orbit, nerve nucleus, or neuromuscular junction (myasthenia gravis)
• Nuclear CN III palsy can not exist without contralateral involvement (contralateral ptosis and SR weakness)

CN III: Anatomic Course
• Fascicles pass through parenchyma of midbrain through Red Nucleus and Corticospinal Tract
  • A lesion, which involves the CN III fascicles as they pass through the Red Nucleus, will cause CN III palsy with a contralateral intention tremor and ataxic gate. This is termed Benedickt’s syndrome.
  • A lesion which involves the CN III fascicles as they pass through the Corticospinal tract will result in a CN IIII palsy with a contralateral hemiplegia. This is termed Weber’s syndrome.
• Exits midbrain into subarachnoid space between cerebral peduncles between superior cerebellar artery and posterior cerebral artery and follows posterior communicating artery
• Enters the lateral wall of cavernous sinus where it bifurcates into superior and inferior divisions just before exiting cavernous sinus
• Enters the superior orbital fissure where it further divides to innervate the individual muscles
• CN III is vulnerable to compression by aneurysm along course of posterior communicating artery or at tip of basilar artery
• Pupillomotor fibers are peripheral in nerve and prone to compression, but relatively immune to ischemia

CN III Palsy: Still More Clues
• A dilated pupil means compression by aneurysm (emergency!)
  • A sudden onset CN III palsy with a dilated, poorly responsive pupil is most likely to be caused by an aneurysm
• Pain can mean anything
• Aneurysms are always painful
  • Boring pain
• Ischemic vascular infarct is painful 90%
  • Retro-orbital pain
• A spared pupil does not always rule out aneurysm
  • There have been 7 cases reported where the pupil was initially uninvolved, but the etiology was an aneurysm. Most of these cases were partial CN III palsies that worsened and became pupil involving over 1 week. Watch these patients daily over one week. Never dilate CN III palsy
• An involved pupil does not rule out ischemia
  • In extreme infarcts, the pupil may be involved as well. These cases are in older patients with vascular disease and are complete CN III palsies
• In a patient with a paresis (incomplete palsy), you can not call the pupil
There is likely an incipient aneurysm growing. A spared pupil does not rule out a life-threatening emergency here.

- CN III palsy caused by aneurysm
  - 20% die within 48 hrs from rupture
  - 50% overall die
  - Average time from onset to rupture – 29 days
  - 80% rupture w/i 29 days
  - Many never make it to hospital
  - Ruptured aneurysms
  - 5% surgical mortality
  - 60% functional impairment post-op
  - Unruptured aneurysms
  - No mortality; 75% with normal outcomes; 50% with CN III recovery
  - Pupil involved CN III palsy = aneurysm of PCA until proven otherwise
  - Complete external dysfunction CN III palsy with normal pupil (pupil spared) is not likely to be an aneurysm & is likely to be vasculopathic
  - Ischemic palsy that will resolve with observation alone
  - Partial internal dysfunction (relative pupil sparing, anisocoria but reactive pupil) = intermediate but unknown risk of aneurysm
  - Dilated pupil alone (internal dysfunction but no external dysfunction) is NOT a CN III palsy
    - Isolated dilated pupil in an ambulatory patient (with no ocular motility deficits) is not an aneurysm, but much more likely to be from iris trauma, medication/pharmacologic dilation, or tonic pupil

**Imaging of CN III palsy**

- Digital subtraction angiography is gold standard and should be done when aneurysm highly suspected
- CT/CTA is preferred non-invasive imaging for CN III palsy
- CT to identify subarachnoid hemorrhage (SAH)
- CTA requires contrast- renal impairment prefers MRI/MRA
- CTA superior to MRI when patient can’t have MRI
  - Pacemaker, claustrophobia
- MRI superior for non-aneurysmal causes (tumor)
- MRA adds very little time to scan

**CN III Palsy: Aberrant Regeneration**

- When damage to the CN III results in a resprouting and miscommunication of nerves to muscles
- Inferior rectus and medial rectus communicates with levator
- Medial rectus communicates with pupil
- Clinical picture:
  - Patient looks medial: lid elevates
  - Patient looks lateral: lid lowers
Patient looks down: lid elevates (Pseudo-Von Graefe’s). This typically is the most identifiable sign in primary or secondary aberrant regeneration

Patient looks medial: pupil constricts

**CN III Palsy: Two Types of Aberrant Regeneration:**

- **Primary:** Occurs independent of antecedent CN III Palsy. Caused by aneurysm or meningioma within cavernous sinus
- **Secondary:** Occurs after an antecedent CN III palsy. Causes:
  - Aneurysm within subarachnoid space, trauma, tumor, inflammation
  - NEVER DIABETES! If cause of CN III palsy is determined to be ischemic vascular (diabetes, HTN, etc.) and then the eye undergoes aberrant regeneration, the initial diagnosis is wrong. You must re-examine for tumor or aneurysm within ipsilateral cavernous sinus.

**Horner’s syndrome**

- An interruption of the oculosympathetic nerve supply somewhere between its origin in the hypothalamus and its termination in the eye.
- The classic findings associated with Horner’s syndrome are ptosis, pupillary miosis, and facial anhydrosis.
- Sympathetic innervation to the eye involves a continuous pathway involving three neurons. The first neuron (considered a central neuron) originates in the dorsolateral hypothalamus, descending through the brain stem and travelling to the ciliospinal center of Budge, between the levels of the eighth cervical and fourth thoracic vertebrae (C8-T4) of the spinal cord. It then synapses with the second neuron (which is considered pre-ganglionic) whose cell bodies give rise to axons, which exit the white rami communicantes of the spinal cord via the anterior horn. These axons pass over the apex of the lung and enter the sympathetic chain in the neck, synapsing in the superior cervical ganglion. At this point the third neuron gives rise to post-ganglionic axons that course to the eye to form the long and short posterior ciliary nerves. These sympathetic nerve fibers course anteriorly through the uveal tract and join the fibers of long posterior ciliary nerves to innervate the dilator of the iris.
- Sympathetic fibers also innervate the muscle of Müller, responsible for initiating eyelid retraction during eyelid opening. Damage at any location along this pathway (central, pre-ganglionic or post-ganglionic) will induce an ipsilateral Horner’s syndrome.
- The diagnosis and localization of Horner’s syndrome can be accomplished with pharmacological testing.
  - In this dysfunction, there is a lack of the sympathetic neurotransmitter norepinephrine. The iris dilator does not receive sympathetic stimulation in Horner’s syndrome, thus accounting for the miosis which increases in dim light conditions and the dilation lag (relative to the normal contralateral pupil) when the lights go down.
  - Previously, topical cocaine was used to identify if Horner’s syndrome was present and hydroxyamphetamine was used to differentiate a third order from a first/second order lesion. However, these drugs are not readily available for clinical practice.
Apraclonidine is a viable replacement. Apraclonidine (0.5% and 1%) is an alpha-2 adrenergic agonist which seems to also stimulate alpha-1 receptors to a negligible degree. Pupil dilation in suspected Horner’s syndrome is considered diagnostic. The theory is that the Horner’s syndrome pupil undergoes denervation hypersensitivity. When a very weak alpha-1 adrenergic agonist is applied, the hypersensitive pupil dilates while the normal pupil has no effect. In most cases, there will actually be a reversal of the anisocoria, which is easier to appreciate than the asymmetric dilation induced by cocaine. It appears that the most readily available agent, apraclonidine 0.5% (Iopidine) is at least as sensitive and specific in the diagnosis of Horner’s syndrome as is cocaine.

- Localizable- targeted workup
  - Neck and facial pain ipsilaterally- carotid dissection
  - Facial paraesthesia- middle cranial fossa disease

Necessary Work Up (non-localizable):
  - MRI of brain, orbits and chiasm with and without contrast, attention to middle cranial fossa.
  - MRA of head and neck-rule out carotid dissection
  - MRI of neck and cervical spine, include lung apex and brachial plexus
    - Horner’s syndrome patient needs to be imaged from chest to head-3 scans
    - Horner’s protocol
  - A 3rd-order Horner’s and ipsilateral head, eye, or neck pain of acute onset should be considered diagnostic of internal carotid dissection unless proven otherwise.
  - Carotid artery dissection presents with the sudden or gradual onset of ipsilateral neck or hemicranial pain, including eye or face pain
    - Often associated with other neurologic findings including an ipsilateral Horner’s syndrome, TIA, stroke, anterior ischemic optic neuropathy, subarachnoid hemorrhage, or lower cranial nerve palsies
  - Horner’s from suspected carotid dissection should immediately go to hospital emergency room/ emergency department
VEP & ERG: Electrodiagnostics in Clinical Practice: Patient Wins, Practice Wins

Nathan Lighthizer, O.D., F.A.A.O
Assistant Professor, NSUOCO
Chief of Specialty Care Clinics
Chief of Electrodiagnostics Clinic

Course Outline/Objective
- What is electrodiagnostics testing?
- Visual Pathway – Basic Understanding
- VEP
- ERG
  - Full field flash
  - Pattern
  - mfERG
- EOG
- Clinical Cases

Visual Pathway
- Upstream
  - Photoreceptors
  - Mid-retinal layers
  - Ganglion cell layer
  - NFL/Optic Nerve
  - Optic Chiasm
  - Optic Tract
  - LGN
  - Visual Cortex
- Downstream
The Visual Evoked Potential (VEP) objectively measures the functionality of which structure?

A. Photoreceptors  
B. RPE layer  
C. Ganglion cell layer  
D. Nerve fiber layer & optic nerve  
E. Entire visual pathway

Which of the following is an indication to perform a VEP?

A. Glaucoma  
B. Traumatic brain injury  
C. Optic neuritis  
D. Amblyopia  
E. Unexplained vision loss  
F. VF defect  
G. All of the above

Visually Evoked Potential (VEP)

- AKA Visually Evoked Response (VER)
  - Flash vs. Pattern

- Measures the entire visual pathway
  - From cornea to occipital lobe

- 3 electrodes
  - Ground
  - Reference
  - Measuring -> occipital lobe
    - 1" above inion
Many optic nerve diseases are asymptomatic because central vision is not affected until late in the disease. Diagnosis and management of optic nerve disorders are often based on structural or subjective visual field tests. VEP is an objective, functional test that can help discriminate between healthy and glaucomatous eyes.

**VEP and Glaucoma: Well Defined Science**

The Visual Evoked Potential in Glaucoma and Ocular Hypertension: Effects of Check Size, Field Size, and Stimulation Rate


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“Increased pattern VEP latency was significantly correlated with both the severity and location of visual field defects and the degree of cupping and pallor of the optic disc.”

The authors of this paper are world-recognized electrophysiology specialists from the New England Medical Center and University of Chicago.

---

“The finding that is of clinical importance is the presence of abnormally long VEP latencies in some patients with ocular hypertension. The abnormal prolongation of VEP latency in these eyes may reflect subclinical optic nerve lesions that have not been uncovered with other techniques.”
Additional Clinical Papers


Many optic nerve diseases are asymptomatic because central vision is not affected until late in the disease.

Diagnosis and management of optic nerve disorders are often based on structural or subjective visual field tests.

VEP is an objective, functional test that can help discriminate between healthy and glaucomatous eyes.

Low contrast testing demonstrates degradation of magnocellular pathways:
- An early indication of glaucoma.

High contrast testing demonstrates degradation of parvocellular pathways:
- An early indicator of central vision loss and issues caused by problems before signal reaches optic nerve.

**patient should be tested with best corrected vision**

Main Indications:

- Glaucoma
- Glaucoma suspects
- Multiple Sclerosis
- Ischemic Optic Neuropathy
- Traumatic Brain Injury
- Amblyopia
- Other Neuropathies
- Unexplained vision loss
- VF defect
- FDT
ERGs are electrical signals that are a measure of the electrophysiological activity at the retina. **Mid-retinal layers, ganglion cell layer, and nerve fiber layer**

- Objectively measures retinal function
- ERGs can help improve sensitivity and specificity in diagnosing optic neuropathies and maculopathies like glaucoma and macular degeneration when used in conjunction with other tests
- Can also help the clinician differentiate between retinal and optic nerve disorders when used in conjunction with Visual Evoked Potential (VEP).

### Pattern ERG (pERG)

- Concentric Stimulus Fields
  - Drug toxicity
  - Diabetic macular edema
  - AMD
- Contrast Sensitivity
  - Glaucoma
  - Diabetic retinopathy
1. Concentric Stimulus Fields
   - Stimulus delivered at 15 flips/second
   - BCVA
     - Pt should be properly refracted for 24”
   - 24” testing distance
   - 100% contrast
   - Right eye (OD) then Left Eye (OS)
     - 25 seconds at 24 degrees
     - 25 seconds at 16 degrees

2. Contrast Sensitivity
   - Stimulus delivered at 15 flips/second
   - BCVA
     - Pt should be properly refracted for 24”
   - 24” testing distance
   - 85% and 15%
   - Right eye (OD) then Left Eye (OS)
     - 25 seconds at High Contrast (Hc)
     - 25 seconds at Low Contrast (Lc)

“...In patients who are glaucoma suspects, pERG signal anticipates an equivalent loss of OCT signal by several years (as many as 8 years)."

“In patients who are glaucoma suspects, pERG signal anticipates an equivalent loss of OCT signal by several years (as many as 8 years).” Invest Ophthalmol Vis Sci. 2013;54:2346-2352. DOI:10.1167/iovs.12-11026
pERG Indications

- Glaucoma
- Optic Neuropathies
- Maculopathies
  - AMD
  - Diabetic retinopathy
  - Diabetic macular edema
  - Macular toxicity

pERG Testing

Pattern ERG (pERG)
Pattern ERG (pERG)

Applying to Your Practice

**VEP**
1. Glaucoma & glaucoma suspects
2. Unexplained vision loss
3. Transient vision loss
4. Unexplained VF defects
5. Unreliable VF
6. Optic neuropathies
7. Optic neuritis/MS
8. Amblyopia
9. TBI

**PERG**
1. Glaucoma & glaucoma suspects
2. Unexplained VF defects
3. Unreliable VF
4. Optic neuropathies
5. Maculopathies
6. AMD
7. Diabetic macular edema
8. High risk med use (Plaquenil)
9. Generalized DR

**FLASH ERG**
1. RP & its variants
2. Cone dystrophies & Rod monochromat
3. Symptoms:
   - "Night blindness"
   - Restricted peripheral fields
   - Color vision deficits

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Normal</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>VEP</td>
<td>100</td>
<td>75</td>
<td>50</td>
<td>25</td>
</tr>
<tr>
<td>PERG</td>
<td>50</td>
<td>25</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>FLASH ERG</td>
<td>25</td>
<td>10</td>
<td>5</td>
<td>2</td>
</tr>
</tbody>
</table>
New Innovations in Surgical Eye Care

Jim Owen, OD, FAAO
Encinitas Optometry
nJoy Vision

Disclosures

- Jim Owen, OD
- TearLab
- VMAX
- Allergan
- AMO
- Alcon
- Tear Science
- Tear Film Innovations

Ectasia Diagnosis
Screening Patients for Refractive Surgery

- Goal is to detect all patients who are susceptible to keratectasia
- Corneal topography and tomography can only detect keratectasia once it has begun.
- Corneal tomography can detect earlier changes occurring on the back of the cornea
- Biomechanical changes may occur before any topographic and tomographic changes

Evolution of Corneal Topography

- Curvature
- Elevation - Slit scanning
- Elevation - Scheimpflug

Pentacam - Enhanced Ectasia Display

- Normative Database > 1400 eyes
Belin-Ambrosio Enhanced Display

- Combined elevation analysis with an enhanced best fit sphere combined with pachymetric progression analysis increases the detection of early forms of corneal ectasia.\(^1\),\(^2\),\(^3\).

- Multivariate regression analysis increases the sensitivity and specificity of early ectasia detection to 98\%.\(^4\).

4. Ambrosio R, Belin m. The BAD may be better for detecting ectatic disease and its susceptibility Eurotimes Jan. 2010
Goals

To provide the practicing optometrist details regarding CXL for keratoconus and kerato-ectasia.

Safety and Efficacy

Patient Selection

N= 81,715 Consecutive Eyes – Apr 08 thru Mar 09
Femtosecond and Mechanical flaps
CCT <500 – 2181 eyes  CCT >500 - 79534

Ectasia has been observed in 11 Patients

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>CCT (µm)</th>
<th>Th (µm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>29</td>
<td>562 / 562</td>
<td>341 / 341</td>
</tr>
<tr>
<td>2</td>
<td>31</td>
<td>542 / 548</td>
<td>382 / 409</td>
</tr>
<tr>
<td>3</td>
<td>24</td>
<td>533 / 540</td>
<td>369 / 364</td>
</tr>
<tr>
<td>4</td>
<td>29</td>
<td>545 / 540</td>
<td>341 / 349</td>
</tr>
<tr>
<td>5</td>
<td>32</td>
<td>521 / 527</td>
<td>302 / 280</td>
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<tr>
<td>6</td>
<td>21</td>
<td>537 / 537</td>
<td>314 / 319</td>
</tr>
<tr>
<td>7</td>
<td>23</td>
<td>498 / 493</td>
<td>267 / 262</td>
</tr>
<tr>
<td>8</td>
<td>25</td>
<td>527 / 527</td>
<td>318 / 345</td>
</tr>
<tr>
<td>9</td>
<td>25</td>
<td>535 / 540</td>
<td>300 / 307</td>
</tr>
<tr>
<td>10</td>
<td>29</td>
<td>524 / 530</td>
<td>318 / 315</td>
</tr>
<tr>
<td>11</td>
<td>29</td>
<td>522 / 520</td>
<td>310 / 318</td>
</tr>
</tbody>
</table>

Cross-Linking Principle: Strengthening the Cornea

328.9% increase in the rigidity of the human cornea! 1,2

Healthy Cornea

A healthy cornea retains its shape due to strong crosslinks between the collagen fibers.

Corneas with KCS

In corneas with signs of keratoconus collagen is lost and crosslinks are diminished.

The cornea weakens and bulges.

Collagen Cross Linking

Corneal collagen crosslinking (CXL) with riboflavin strengthens the weakened structure by adding collagen crosslinks.
Collagen Cross-linking (CXL)

- Process well known in material science
- Addition of molecular bonds to increase mechanical strength of tissue
- Enzymatic process

Cross-links can be induced enzymatically, by means of:

<table>
<thead>
<tr>
<th>Aldehydes</th>
<th>Chemical Fixatives</th>
<th>Photosensitizing Radiation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose</td>
<td>Glutaraldehyde</td>
<td>Riboflavin/UVA</td>
</tr>
</tbody>
</table>


Methods of CXL

- Glutaraldehyde crosslinking (prosthetic heart valves)
- Formaldehyde (pathology specimens)
- Aldehyde sugars (diabetes)
- UVA-induced crosslinking (dentistry)

UVA CXL BASICS

1. Riboflavin (vit. B2) + Ultraviolet radiation
2. Production of oxygen radicals (ROS)
3. Induction of collagen cross-links
**COLLAGEN**

A Complex Family of genetically distinct proteins
- 13 Sub-types
- 3 helical alpha chains forming fibrillar Triple Helix
- X Linking confers stability increasing tensile strength
- Initiated by Lysyl Oxidase

---

**Understanding UVA Corneal Crosslinking**

- UVA- Long wave UV
  - 400-300nm
  - 3.10-4.13ev/photon
  - CXL
-295-297nm
-UVB
-Medium Wavelength

**ULTRA VIOLET LIGHT**

**Electromagnetic Radiation**
- Wavelength shorter than visible light
- 10-400nm
- Photon energy 3eV-124eV/photon
- Higher energy wavelengths ionizing extreme ultraviolet
- Power to alter chemical bonds
- 97% blocked by ozone layer

---

**Background of Corneal Crosslinking**

<table>
<thead>
<tr>
<th>Year</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>2004</td>
<td>Collagen fiber diameter in the rabbit cornea after crosslinking by riboflavin/UVA. Wollensak G, Wilsch M T, Seiler T. Cornea; 23: 503-507</td>
</tr>
</tbody>
</table>
Regulatory Status

International
- CE Mark
- Distributed internationally

United States
- ORPHAN DRUG STATUS FOR Avedro VibeX
  - Announced Sept 12, 2011 for treatment of keratoconus
  - Announced Dec 19, 2011 for ectasia following refractive surgery
- Combination product
  - Device: UVA light source
  - Drug: Riboflavin

Cross-Linking: Techniques

Epithelium OFF vs Epithelium ON

Riboflavin is used during CXL because it increases the absorption of UV-A light by the cornea.1,2

The more UV-A light that is absorbed, the greater the effect of crosslinking.

An added benefit is that the riboflavin helps to protect the endothelium and intraocular tissues from UV-A exposure.

SAFETY

The wavelength of UV-A light is between 320 and 340nm.

The typical UV-A dose on the surface of the cornea is 5.4 J/cm², a similar dose to what the cornea would receive after 15 to 20 minutes of sun exposure on a summer day.


UV A Corneal Absorption in Presence of Riboflavin

<table>
<thead>
<tr>
<th>Irradiance</th>
<th>Damage Threshold</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.00 mW/cm²</td>
<td>Keratocytes: 0.5 mW/cm²</td>
</tr>
<tr>
<td>1.49 mW/cm²</td>
<td>Endothelium: 0.3 mW/cm²</td>
</tr>
<tr>
<td>0.74 mW/cm²</td>
<td></td>
</tr>
<tr>
<td>0.36 mW/cm²</td>
<td></td>
</tr>
<tr>
<td>0.18 mW/cm²</td>
<td></td>
</tr>
<tr>
<td>0.09 mW/cm²</td>
<td></td>
</tr>
<tr>
<td>0.06 mW/cm²</td>
<td></td>
</tr>
</tbody>
</table>

Epithelium-off

EPI OFF: When the epithelium is removed, this is done prior to the application of riboflavin, and corneal exposure to UV-A light. The healing process is similar to that of PRK, including the option to place a bandage contact lens to promote healing.

* Some surgeons argue that epithelium-off treatments are riskier, in part due to the possibilities of corneal infection associated with the lengthy healing process (4 to 6 days) and corneal haze.

An alternative 3,4 is to apply the riboflavin over the intact corneal epithelium. This is followed by corneal exposure to UV-A light. Visual recovery is faster with this approach, and there are lower risks for infection and haze.

Treatment takes longer, because the cornea does not absorb the riboflavin as quickly.

Surgeons are still assessing which provides the greater degree of crosslinking.

---

**EPI ON**

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---

**Immunofluorescent Staining Confocal Microscopy**

**J Refract Surg 2008 (Sept); 24(7): S715-9**

**NO STROMAL COMPACTION IN PRESENCE OF EPITHELIAL OR WITHOUT UV OR RIBOFLAVIN**

---

**Cornea A** - CXL with the epithelium on.

Minimal stromal hypereflectivity in the stroma-less CXL effect

**Cornea B** - Athens Protocol. Note vast hyperreflectivity of the stroma up to 300 microns with broad diameter of effect

---

**CXL EFFECT EPI-ON/EPI-OFF**

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---
Figure 1. (A,B) The demarcation line is visible in these clinical images. (C) Visante OCT confirms the depth of the demarcation line.

What If You Could Change The Power Of An IOL and Treat High Order Aberrations After Implantation?

Light Delivery Device
Adding Power to the LAL

<table>
<thead>
<tr>
<th>Iris</th>
<th>light</th>
<th>Iris</th>
<th>light</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

"lock-in"

Increased power

\[ \Rightarrow \text{change in radii of curvature} \Rightarrow \text{change in power} \]

Subtracting Power from the LAL

<table>
<thead>
<tr>
<th>Iris</th>
<th>light</th>
<th>Iris</th>
<th>light</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

"lock-in"

Decreased power

\[ \Rightarrow \text{change in radii of curvature} \Rightarrow \text{change in power} \]

Figure 1. Schematic of the positive power adjustment mechanism. A) Adjustment: selective irradiation of the central zone of the light adjustable lens (LAL) polymerizes the macromer, creating a difference in the chemical potential between the irradiated and nonirradiated regions. B) To re-establish equilibrium, the excess macromer diffuses into the irradiated region causing swelling. C) Lock-in Treatment: irradiation of the entire LAL "locks" the remaining macromer so that no further change of refraction is possible.
Summary

- Silicone Light Adjustable IOLs
  - Myopic, hyperopic, and astigmatic errors
  - Custom Wavefront
  - Platform, Phakic IOL, Multifocal or Accommodative IOL, Injectable IOL

Corneal Inlays
AcuFocus™ KAMRA
Corneal Inlay

- Designed to improve near vision in patients with Presbyopia
- Easily implanted
- Minimal impact on distance vision
- Removable

Central aperture: 1.6 mm
Overall diameter: 3.8 mm

AcuFocus™ KAMRA
How it Works

- The small aperture created by the AcuFocus™ ACI 7000 blocks the unfocused light on the retina

Blocks unfocused light
Allows focused light into the eye

Inlay Design

- Thickness: 5µ
- Weights less than a salt crystal
- Curvature: 7.5 mm radius
- 1.6mm depth
- 8,400 holes (5-11µ)
- 3.8mm overall diameter
Corneal Health

The AcuFocus™ KAMRA Procedure

- Topical anesthetic eye drops
- Flap created
- The AcuFocus™ ACI 7000 is inserted and centered
- The flap is closed
- Takes less than 30 minutes - start to finish
Depth of Focus Simulation

f/5.6 simulates human eye ~ 4.0 mm pupil

f/22 simulates the effect of the Inlay ~ 1.6 mm pupil

iDesign Dx system
An Innovative Approach to Measuring Refractive Errors

- Highly accurate relevant measurements
  - Accurate sphere, cylinder, axis, K values, pupillometry, etc.
  - Spatial, angular and temporal registration of measurements

- Potential to capture highly aberrated eyes
  - Wide refractive range
  - Enhanced patient throughput and ease of use

- Five measurements within a single capture sequence
  - Wavefront aberrometry
  - Wavefront-derived refraction
  - Full gradient corneal topography
  - Pupillometry
  - Keratometry


Wavefront-derived Refraction

- **iDesign Dx** system refractions agree with manifest refractions, but are more reproducible.
  - Advanced Hartmann-Shack sensor
  - Automatic chromatic correction
  - Vertex variation is automatically compensated using a novel rangefinder
  - Fogging sequence automatically adjusts according to patient astigmatism

1. Eugenia Thomas, OD; T.D. Raymond, PhD, Sheila Stevens, Amelia Saliba, Sanjeev Kasthurirangan, BSOpt, PhD, Performance of a new high density Wavefront Aberrometer (iDesign system); ME6988.

2. Charles CE, Raymond T.D, Baer CD, Neal DR Comparison of repeatability of manifest refraction and instrument-based refraction. ARVO 2012; RD3123

3. Ron Rammage, D.R. Neal, James Copland, TD Raymond, Wei Xiong, Steve Farrer, Phil Riera, Comparison of automatic fogging methods to minimize accommodation, ARVO 2012; RD4897.

iDesign Dx vs WaveScan system sensor comparison

<table>
<thead>
<tr>
<th>Parameter</th>
<th>WaveScan system</th>
<th>iDesign Dx system</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hartmann-Shack Sensor</td>
<td>400 um</td>
<td>177 um</td>
</tr>
<tr>
<td>Lenslet Size</td>
<td>241 lenslets (7mm pupil)</td>
<td>2257 lenslets (7mm pupil)</td>
</tr>
<tr>
<td>Refractive Range</td>
<td>-8 to +6 D</td>
<td>-16 to +12 D</td>
</tr>
<tr>
<td>Sphere Cylinder</td>
<td>0 to 6 D</td>
<td>0 to 8 D</td>
</tr>
<tr>
<td>SEQ Pre compensation</td>
<td>Badal Optometer</td>
<td>Badal Optometer</td>
</tr>
<tr>
<td>Cyl Pre compensation</td>
<td>Opto-mechanical</td>
<td>None required</td>
</tr>
<tr>
<td>Chromatic Correction</td>
<td>None Applied</td>
<td>Automatically Applied</td>
</tr>
</tbody>
</table>

High dynamic range Hartmann-Shack sensor eliminates need for cylinder pre-compensation
Fogging sequence adjusts according to astigmatism

- WaveScan System
  - Fogging sequence is a step function
  - Fogging amount is constant for all subjects

- iDesign Dx System
  - Fogging sequence is a controlled ramp (2 D/sec)
  - Fogging amount increases for subjects with high astigmatism

---

How important is chromatic aberration?

- Dispersion in the eye causes refraction values to depend on the wavelength of measurement
- Without correction for chromatic aberration, near infrared auto‐refractors would report “over plus” compared to manifest refraction
- iDesign Dx system refractions are automatically corrected for chromatic aberration to agree with manifest refraction

---

to compensate variation in eye distance.

- Distance to eye is measured with a proprietary rangefinder
- Inner ring positions vary with eye distance
- Helmholtz spot positions are independent of eye distance
- Refraction is corrected accordingly
- This correction can be important for subjects with high refractive error
extremely well correlated to manifest refraction

Wavefront Aberrometry

- High-definition Hartmann-Shack wavefront sensor provides five times higher spatial resolution than WaveScan system\(^1\)
- High-dynamic-range Hartmann-Shack wavefront sensor provides eight times higher local slope range than WaveScan system\(^1\)
- Each spot is tested using a patented qualification method\(^2\) before being included in the wavefront reconstruction

Resolution and dynamic range are important when measuring highly aberrated eyes
Five measurements on a single capture sequence

Wavefront-derived refraction

Wavefront Aberrometry

Pupillometry

Full Gradient Corneal Topography

Keratometry

Full Gradient Topographer vs. Placido Disk

- Placido Disk Topographers
  - Pervasive in the industry; well understood; familiar
  - Well developed algorithms
  - However
    - Skew rays are not directly captured
    - More sensitive to the radial component of the gradient
    - Topography maps are not accurate in some cases

- Full Gradient Topographer
  - Provides central cornea coverage
  - Captures both x and y slopes for each spot
  - Reconstruction of the corneal elevation is much like Shack-Hartmann sensor methods
  - Potential for increased accuracy
  - Not inherently sensitive to misaligned eyes

The iDesign Dx system cone is designed to cast a nearly uniform grid of measurement spots on normal eyes
Keratometry
- Calculated from corneal topography data
- Accurate to within 0.25 D

Full Gradient Corneal Topography
- Specifications Include:
  - Zonal reconstruction and 8th order Zernike reconstruction
  - Coverage > 8.3 mm*
  - Axial Power Accuracy better than 0.25 D**
  - Axial Power Repeatability < 0.15 D**

*Coverage based on an 8.0 mm radius of curvature sphere.
**Measuring known test calibration spheres.
iDesign Dx dual wavelength eye illumination results in brighter eye images with higher contrast than WaveScan system.

WaveScan system

iDesign Dx system

Pupillometry

- Measures pupil diameter under controlled scotopic and photopic lighting conditions

Scotopic Image
< 3 cd/m²

Photopic Image
> 85 cd/m²

© 2013 Abbott Medical Optics Inc.

9th Innovation

Femto-Assisted Corneal Surgery

© 2013 Abbott Medical Optics Inc.
Femto-Intacs Advantages

- Less surgeon dependent
- Reduced risk anterior/posterior perforation
- Increased reduction in HOA (increased BCVA)
- More precise placement
- More effect
  - Easier to center on pupil
  - Faster vision recovery
  - Less pain
  - Greater patient satisfaction!


Intacs for Keratoconus
IntraLase Enabled Keratoplasty

History: Advanced Shaped PK

- Similar technique to the posterior two-level graft
- Adapted from modern day penetrating keratoplasty using modern instruments

Valve-Sealing Edge Design

Prevents Leakage

Intraocular Pressure

Suture Not Tight
The Zig-Zag shaped incision has shown a smooth corneal contour immediately after surgery with less distortion of the corneal optics and less astigmatism.

*Personal communication, Roger Steinert, M.D.*
Astigmatism

Typical 1 yr post-op result with standard trephine cut PKP = 8 diopters of astigmatism

IntraLase Advanced Keratoplasty at 3 months post-op = ½ diopter of astigmatism

IEK Surgical Video

BENEFITS OF FEMTO-AK

- Incomparable safety
- Decisive control of all surgical parameters
- Fully computerized control
- Maximal patient comfort
- Minimal learning curve
- Precision & predictability in the creation of AK resections ± 10 Microns
FEMTO-AK PROCEDURE

Docking procedure
FEMTEC Laser

Femto-AK Conclusions

- The correction of astigmatism with the femtosecond laser is safe and effective 1,2

- Femtosecond assisted astigmatic keratotomy is more predictable and can correct more astigmatism than mechanized astigmatic keratotomy3.


Surgical Applications

- Presbyopia Correction
  - Photo-disruption within the lens to restore flexibility and the ability to accommodate
  - Peripheral lens incisions (enhanced lens elasticity)
Dropless Therapy
Proprietary Sterile Injectable Compounded Formulations

The modality of "Dropless" therapy involves the injection of an eye-compatible compound at the end of the cataract case as prophylaxis against inflammation and infection.

Currently, there are 2 combinations available only from Imprimis:

- **Tri-Moxi**: triamcinolone acetonide and moxifloxacin hydrochloride
- **Tri-Moxi-Vanc**: triamcinolone acetonide, moxifloxacin hydrochloride and vancomycin

Novel Patent-Pending Formulations†

Imprimis' Dropless therapy is the only commercially-available solution for a single injection of anti-infective and anti-inflammatory prophylaxis.

- Proprietary technology allows for the unique combination of these drugs. The resulting small, consistent particulate size enables injection through a 27-30 gauge needle or cannula.
- The formulations have been optimized for the isotonicity and pH most compatible with the eye.

†Comprised by a pharmacist pursuant to a prescription to meet the needs of individual patients.
PATIENT JOURNEY: DROP THERAPY

**Cataract Patient Profile**
- 80 years old
- Arthritic hands + Scoliosis
- Lives alone + Fixed income

**Patient Surgery**
Scheduled for cataract surgery, with pre- and post-operative topical medications.

**Day of Surgery**
Patient shows up with QID generic drops, as prescribed by MD. Informed about dropless therapy.

**1 Week Post-Operative**
Patient is given compound anti-inflammatory and anti-infective medication, injected intravitreally at the end of the cataract case intended to last the duration of the postoperative period.

**1 Month Post-Operative**
Eye looks quiet, no infection, no inflammation.

**Patient Experience**
Calls office repeatedly, confused, and asking for help. MD questions efficacy of medications due to compliance issues.

Minimized risk of endophthalmitis and inflammation.

---

PATIENT JOURNEY: DROPLESS THERAPY

**Cataract Patient Profile**
- 80 years old
- Arthritic hands + Scoliosis
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**Patient Surgery**
No pre- or post-operative drops prescribed.

Informed about dropless therapy.

**Day of Surgery**
Patient is given compound anti-inflammatory and anti-infective medication, injected intravitreally at the end of the cataract case intended to last the duration of the postoperative period.

**1 Week Post-Operative**
Eye looks quiet, no infection.

**1 Month Post-Operative**
Patient happy with outcome.

MD not concerned about compliance issues.

Minimized risk of endophthalmitis and inflammation.

*Compounded by a pharmacist pursuant to a prescription to meet the needs of individual patients. May be customized. Some patients may need drops.

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Dropless Therapy Patient Benefits

- Support physically and/or mentally challenged patients
- Eliminate compliance challenges of proper dosing
- Lift burden from family members/caregivers assisting with instillation
- Put patients with "Eye Drop Phobia" at ease
- Avoid pharmacy issues: premature refills, generic switches, QID/BID dose alterations
- Help extended care patients in nursing facilities
- Aid patients without insurance, money or access to sample drops

- Osteoarthritis
- Rheumatoid Arthritis
- Sciatic
- Parkinson’s
- Hypothyroid
- Alzheimer’s
- Dementia

- Drop Therapy with branded medications can cost over $400
Video

Thank You!
Welcome to the Professional Responsibilities Course sponsored by the University of Houston College of Optometry. As you know, this course is a requirement for Texas license holders. What you may not know is that all fees associated with this course are devoted to permanent projects that are important for the future of the profession.

Thank you for choosing UHCO for your continuing education.

The development and production of the 2015 Professional Responsibility Course is underwritten by the Harris Lee Nussenblatt Lecture Series Endowment. This endowment was established in 1992 by the Nussenblatt Family in memory of former Associate Professor Harris Nussenblatt, OD.

The Lecture Series focuses on issues related to professional ethics, public health and practice administration.
Preface

The content of the Professional Responsibility Course is at the discretion of the Texas Optometry Board. This year, the Board requested only a few issues be addressed. The rest of the agenda will address the core concept of this course, professional ethics.

UHCO and the Coursemaster thank the following leaders of our profession for their contribution and advice in developing this years program: Ron Hopping, Jeff Jones, Clarke Newman, Stacie Virden, Peter Cass, Laurie Sorrenson, Kevin Katz, and Bj Avery. Special thanks to Clarke Newman for his research and invaluable opinions and to Jeff Jones for supplying the title of the course.

AGENDA I – TEXAS OPTOMETRY BOARD

Drug prescribing information
- New classification of Schedule II Drugs
- Reference for pain management drugs
- Rules 280.5 and 280.10 listing types of drugs that may be prescribed

Professional designation
Importance of reading newsletter
Issues with EHRs
New Rule 277.10 – Remedial Plans

AGENDA II – SITUATION ETHICS

What are the challenges in ethical behavior

Examples of challenges in ethical behavior
New Drug Prescribing Information
Reclassification of Hydrocodone to Schedule II

- Implementation Dates
  - October 6, 2014 – the actual adoption date
  - April 8, 2015 – the actual implementation date for the majority of the regulation changes

- What this really means for Texas ODs
  Optometrists in Texas cannot prescribe Schedule II narcotics and most all pharmacies are already using the adoption date as the implementation date. You must find alternate sources of pain management for your patients.

New Drug Prescribing Information
Misc. Issues

- To find or look up the classification of any controlled substance – reference www.dea.gov/druginfo/ds.shtml or www.deadiversion.usdoj.gov/schedules

- You can find a good deal of information on controlled substances, drug abuse and patient diversion tactics at http://www.pharmacy.texas.gov/sb144.asp

- To review the medications that you are allowed to prescribe under current Texas law, reference www.tob.state.tx.us, specifically Rules 280.5 and 280.10

Practice of License Holder
Professional Identification

The Statute: Section 351.362
Rules: Rule 279.10

Name(s) of the optometrists practicing at a location must be visible before entry into the reception area

Does not apply to doctors acting in a temporary capacity as defined in the rule as “no more than two consecutive months”
Practice of License Holder Professional Identification

Legal identification per state law includes:
- Optometrist
- Doctor, Optometrist
- Doctor of Optometry
- O.D.

It is illegal to use any designation or advertising that could mislead the public into thinking you are any other health care practitioner other than an optometrist. This is not the Optometry Board’s law – this is a State law the Optometry Board must uphold.

www.statutes.legis.state.tx.us/Docs/OC/htm/OC.104.htm

Texas Optometry Board Newsletter

- The Optometry Board releases a newsletter once a year to all licensees. The newsletter identifies issues the Board feels are important to all practicing optometrists as well as explanations of all new Rules passed since the last newsletter.
- You are legally obligated to stay abreast of and follow the law. “Ignorance” is not an excuse.
- The newsletter is the easiest way to keep up with any new laws or rules and you are encouraged to read it “cover to cover”. If you are not receiving the newsletter, contact the Optometry Board.

Texas Optometry Board  512-305-8500

Electronic Medical Records

- This is really easy folks. You cannot put statements into a record that do not accurately reflect the services you provided on that date of service.
- Since wellness or routine care examinations can often reveal very little to no change from visit to visit, it is imperative your documentation, that will often look very similar year to year, be representative of the care delivered during that date of service.
- Additional documentation such as review of history statements and/or attestation statements are a good means of making it clear your patient’s records are completely accurate and truthful (remember, most all EHRs have an internal audit feature that tracks the time and date of every entry!)
Examination and Medical Records

All optometrists are encouraged to review the examination requirements found under Rule 277.7 that apply to the initial evaluation of a patient where an ophthalmic prescription is generated.

1. An accurate identification of the patient;
2. The date of the examination;
3. The name of the optometrist or therapeutic optometrist conducting the examination;
4. Past and present medical history, including complaint presented at visit;
5. A numerical value of the monocular uncorrected or monocular corrected visual acuity in a standard acceptable format;
6. The results of a biomicroscopic examination of the lids, cornea, and sclera;
7. The results of the internal examination of the media and fundus, including the optic nerve and macula, all recorded individually;
8. The results of a retinoscopy. A tape from an automatic refraactor is acceptable;
9. The subjective findings of the examination. A tape from a computer assisted refraactor/photometer is acceptable if the instrument is being used to obtain subjective findings;
10. The results of an assessment of binocular function, including the test used and the numerical endpoint value;
11. A tonometry reading including the type of instrument used in the examination; and
12. Angle of vision: the extent of the patient's field to the left and right. The initial evaluation of a patient where an ophthalmic prescription is generated

Documentation Notes

Be aware that the Board Rules require that the examining optometrist PERSONALLY make and record the examination elements listed in orange (biomicroscopy, internal evaluation, subjective refraction)

Optometrists should also be aware that, although not a requirement of the Texas Optometry Board, the rule that the attending physician personally “make” the patient’s HPI is commonly cited, while the rest of the history may be delegated to an assistant/technician as long as the it is clear the physician has reviewed the information.
NEW Rule 277.10 – Remedial Plans

- This Rule gives the Board the authority to resolve typically more minor violations by mutual agreement to a remedial plan.
- If the licensee completes the requirements of the remedial plan, the violation is removed from the licensee’s record two years after completion of the remedial plan and is not reported to the national physician data bank.
- Remedial plans may be issued a maximum of once every two years.
- Remedial plans may be initiated by the Executive Director of Investigative Committee but must be approved by vote of the Board.
- Remedial plans may include a $1,000 administrative fee.

And now...

Situation Ethics

Are Ethics a Real Issue?

- We all face “ethical” decisions every day – it’s not limited to what most would consider as lying, immorality, religious beliefs or generally being a “good or bad person.”
- Ethical decisions can range from something terrible like deciding to rob a bank to something seemingly benign like not handing out bonuses to your staff because you really want to buy a new car.
- Our decisions are influenced by a host of internal and external influences.
- Not all decisions have a “right” answer – many are “shades of gray” (thanks Jeff!)

Much of the information in the next few slides can be found in the excellent reference www.ethicsunwrapped@utexas.edu
“Ethics Unwrapped” identifies 22 moral standards that define how we make decisions. The next slides review eight standards considered most applicable to doctors.

### Moral Standards

#### Role Morality
Actions or decisions are justified because of the unique role we play (as doctors) in or because we separate our personal beliefs from our work beliefs.

EX: Selling patient ocular supplements when you wouldn’t take them yourself

#### Conflict of Interest
Actions or decisions are influenced by professional or economic interests

EX: “Stretching” medical necessity (is that specular microscopy REALLY necessary even though it will add to the month’s bottom line)

### Moral Standards

#### Ethical Fading
“What was I thinking?” Decisions are based more on an emotional response than a rational response (“moral disengagement”).

EX: Insider trading with a pharmaceutical company

#### Incentive Gaming
Decisions or actions influenced by potential incentives, usually monetary.

EX: Incentive bonus systems – employed doctors and/or staff

(NOTE: Unwrapped authors define the new American Dream as “minimal effort for maximum gain”)
Moral Standards

Incrementalism
No one wakes up one day and decides to lose their morality. It is almost always a progressive lowering of the ethical bar, often based on prior success with lower standards.
EX: Stretching medical necessity progresses to billing fraud

Moral Equilibrium
Also called “moral licensing” – keeping score on our good behavior allows us to justify a certain degree of behavior we otherwise would not consider acceptable
EX: Indigent care efforts make it reasonable to overbill patients with insurance

Moral Standards

Moral Imagination
Success defined by many as winning. In the movie “Margin Call”, Jeremy Irons says “there are only three ways to win – be first, be smarter or cheat.” When winning rules our lives, our emotional barometer can lead our imagination to find ways to cheat and consider it part of doing business.
EX: Embezzlement

Moral Myopia
Possibly the most common and deadly – it is the “everyone is doing it” scenario. Blurring the right behavior is often fueled by potential for financial gain.
EX: The classic scenario of “run this test – you’ll get paid” forgetting the rule of medical necessity

Again, we must emphasize that not all seemingly straightforward “ethical” decisions are always so clear cut. While some actions are obviously unethical (billing for services not rendered) others can be “shades of gray” (individual decisions regarding medical necessity of care).

With that in mind, let’s look at some “situations” and how they can often be difficult to address.
Situation Ethics – Case One

A fifteen year old patient, cheerleader at her school, presents with an obvious chlamydial conjunctivitis (Effects, at a minimum, 4% of all females 14-19 y/o. Gottlieb – Pediatrics 12/2009). Are you obligated to inform the minor’s parents of this diagnosis and are you required to report this STD to the health department?

The Legal Ins and Outs

➢ In Texas, a minor may consent to treatment of STDs by a physician without parental consent. The attending physician has the authority to decide if the parents have rights to the medical records. (Texas Family Code Title2; Subtitle A; Chapter 32; Subchapter A; Sec. 32.003). The question is does this apply to an optometrist?

➢ In Texas, the attending health care provider is required to report the diagnosis of all STDs to the Texas Department of State Health Services (www.dshs.state.tx.us). This DOES apply to an optometrist.

NOTE: It is widely believed that STDs are significantly under reported!

The Ethical Dilemma

FACT: Treatment and education are essential

➢ Can you just call it an infection and let it go at that?
➢ Can you say you’re not sure of a positive diagnosis and just treat as an infection of “unknown or non-confirmed etiology”?
➢ How do you discuss the situation with the minor in private?
➢ Can you just refer the condition out to someone else?
➢ Is it better to not report and break the law or report and potentially cause real problems for your patient?
So Who Can Get Me?

- The Texas Optometry Board
- The Texas Department of State Health Services
- The minor (the consent issue could be problematic and make it necessary to refer a minor wanting to consent to treatment to a physician as defined by Texas law)
- Yourself – remember your Oath?

"I WILL advise my patients fully and honestly of all which may serve to restore, maintain or enhance their vision and general health."

Situation Ethics – Case Two

One of your highly valued employees is pregnant. She is conducting herself in a manner you feel is detrimental to her health and the baby’s health – smoking, gaining too much weight, drinking heavily on the weekends. What would you do?

The Legal Ins and Outs

- There is no legal requirement or authority on your part. The controlling Texas case on this subject is Collins vs TX, (TX Court of Appeals, 1994). Legally, there must be clear and convincing evidence of mental illness or intent to harm before a woman may be committed to care against her will (FYI – Collins was using cocaine during her pregnancy)
- Firing the employee is very complicated. Texas is an employment at will state but this means little when it come to protected classes like pregnant employees. If the employee pushed for wrongful termination, the suit would be long, painful, expensive and with potential for significant penalty to the employer from an unpredictable jury.
The Ethical Dilemma

➢ Do you have rights as an employer to protect your practice and your employee by counseling the employee on her actions in general and how they may effect her work performance (smoking, drinking, obesity)?
➢ More importantly, do you have a duty as an individual, friend, counselor or humanitarian to discuss the situation with the woman?

So Who Can Get Me?

➢ Your employee - Equal Employment Opportunity Commission and hungry legal counsel will be happy to assist with wrongful termination, gender discrimination, pregnancy discrimination (Pregnancy Discrimination Act of 2014)
➢ Yourself – your duty of care obligations as a health care provider and humanitarian

Situation Ethics – Case Three

A parent brings a child in for an examination. The parent is obviously intoxicated and in no condition to drive. What should you do?
The Legal Ins and Outs

In Texas, this is a no-brainer. See Texas Child Endangerment – Drunk Driving Protection Act. The Act provides a separate mechanism for charging and punishing a person who drives while impaired with a passenger under the age of 15. The statute’s penalties are more severe than Texas’ traditional DWI penalties.

The Ethical Dilemma

- Should you consider the significantly damaging effects conviction of the parent would bring?
- Would providing transportation or a taxi home remove your obligations to report?
- Should you consider the mental trauma the child will go through seeing their parent taken away in cuffs?
- How can you be sure the parent meets the definition of legally intoxicated?

So Who Can Get Me?

- The courts. Failure to report carries potential jail time of 30 days to 5 years and fines ranging from $300 to $10,000, or both.
- The parent – if your assumptions are wrong!
- Yourself – could you live with injury to a child that could have been avoided if you would have reported the potentially dangerous situation?
Situation Ethics – Case Four

One of your employees is strongly suspected of stealing from one or more of your other employees. You feel the only way to get to the bottom of this is make the suspect take a polygraph test. What can/should you do?

The Legal Ins and Outs

- The Employee Polygraph Protection Act of 1988 prohibits employers from “requiring, requesting, suggesting or causing” an employee to take a polygraph test – with exceptions. One of the exceptions is investigation of a crime in your business. There are requirements and regulations involved in these exceptions, a lot of them.
- You cannot take any action against an employee for refusal to take a polygraph test.

The Ethical Dilemma

- How sure are you? If you are that sure, would it be better to find other ways to terminate the employee?
- Can you threaten to polygraph everyone in hope the perpetrator will confess or run? (remember – illegal to “suggest” the polygraph!)
- Provide extra security for your employee’s personal items – like individual lockers
### So Who Can Get Me?

- The “suspect” – if you try to push illegal polygraph testing
- The “suspect” – if you take actions related to their employment that you cannot prove
- Your other employees – unlikely legal action but you have an obligation to protect them

### Situation Ethics – Case Five

Your associate is making false claims to Medicare by up-coding office visits and performing medically unnecessary tests. What should/can you do?

### The Legal Ins and Outs

- The False Claims Act (FCA) allows for treble damages (damages being the fraudulent claim amount) PLUS $11,000.00 fine PER CLAIM
- Fraud is no longer just criminal activity – FCA states that providers “should know” what is medically necessary and should know all billing, coding and reimbursement laws and regulations. Not knowing can now be considered synonymous with fraud.
- The False Claims Act specifically states providers are obligated to self report erroneous billing practices, especially fraudulent activity – even if discovered during a self-audit (new annual Federal requirement for MC/MD providers)
The Ethical Dilemma

- "Self reporting" means you will, at a minimum, pay back the fraud or abuse claims. If the violation is excessive, the addition per claim fine is possible if not likely. This can also easily open the door for a full audit as well as reporting you to all other Federal agencies for potential investigation (all other payers, IRS, DEA, EEOC...you name it, it is "tattle time" in Washington)
- These actions can obviously have significant financial impact on you, your practice and the livelihood of your employees.

So Who Can Get Me

EVERYONE – CMS to start with then the potential reverse funnel to all other payers, IRS, DEA, EEOC. These actions by the Feds are unlikely if you fess up. **BUT THE POTENTIAL RAMIFICATIONS OF NON-DISCLOSURE ARE SEVERE IF NOT FINANICALLY FATAL**

Situation Ethics – Case Six

A patient comes in at 5:00 on Friday with symptoms of flashing lights for the last day. You have plans for the evening, the symptoms do not sound very severe so you conduct a decent but not dilated retinal evaluation using your OptoMap but find nothing. You tell the patient to return in a month. Two weeks later you see them at the mall and they tell you they just had retinal detachment surgery. What would you do?
The Legal Ins and Outs

- Dilated retinal evaluations, especially with symptoms of potential retinal disease present, is a standard of care issue no matter what time of day (See AAO Preferred Practice Pattern “Posterior Vitreous Detachment, Retinal Breaks and Lattice Degeneration” and AOA Optometric Clinical Practice Guideline “Retinal Detachment and Related Peripheral Vitreoretinal Disease”)
- OptoMaps are wonderful but are not a legal substitute for a dilated retinal evaluation (Texas Optometry Board Rule 279.3 (a)(1)(B)

The Ethical Dilemma

Whether the patient actually had a retinal break at the time you evaluated them or not, your care was sub-standard. The only issue remaining is patient management. Suggestions include:
- Do not deny or admit to anything
- Show great concern and compassion
- Isolate but do not alter the medical record in any way

So Who Can Get Me

- The patient – this would be a clear case of negligent care. No one could prove there was a retinal break when you examined the patient but they can easily prove you did not follow standard of care
- Yourself – remember the Oath?

With full deliberation I freely and solemnly pledge that: I will practice the art and science of optometry faithfully and conscientiously, and to the fullest scope of my competence...

I WILL strive continuously to broaden my knowledge and skills so that my patients may benefit from all new and efficacious means to enhance the care of human vision
Situation Ethics – Case Seven

You diagnose a new patient as a significant glaucoma suspect and suggest additional testing. Your patient refuses to proceed with anything their vision insurance doesn't cover and will not give you any medical insurance information. What would you do?

The Legal Ins and Outs

- "Informed Consent" is the responsibility of the doctor. "Informed referral" is the right of the patient. Doctors are very unlikely to be held responsible for the medical consequences of informed refusal if the standards for informed consent are met.
- Sec. 351.360. PROFESSIONAL STANDARD OF THERAPEUTIC OPTOMETRIST. A therapeutic optometrist, including an optometric glaucoma specialist, is subject to the same standard of professional care and judgment as a person practicing as an ophthalmologist under Subtitle B.

The Ethical Dilemma

There really isn’t one. You have three choices:
- Provide comprehensive, documented informed consent – this must include documentation of the risks and potential complications of non-compliance. Continue to follow up with the patient with your best medical recommendations. ATTEMPT TO PIN DOWN WHY YOU HAVE A CARE REFUSAL ISSUE AND SOLVE THAT PROBLEM.
- Give the patient the option of seeing another eye care provider.
- "Divorce" the patient – let’s talk about that concept.
So Who Can Get Me

With proper informed consent, no one. Anyone can attempt to sue you for anything but proper documentation usually prevails. This applies to this patient, the abusive contact lens patient, the patient who won’t take their medication and the like.

Situation Ethics – Case Eight

You are fairly certain you have the flu and are running a fever. You also have a full schedule and are behind on your lab bills. What would you do?

The Legal Ins and Outs

- Texas Optometry Act 351.454(a) - “An optometrist or therapeutic optometrist may not practice optometry or therapeutic optometry while knowingly suffering from a contagious or infectious disease, as defined by the Texas Department of Health, if the disease is one that could reasonably be transmitted in the normal performance of optometry or therapeutic optometry.”
- OSHA/CDC regulations prohibit health care workers with known contagious disease from treating patients if there is likelihood of disease transmission
The Ethical Dilemma

- The responsibility of the world on your shoulders – practice bills to pay, staff members rely on you for income, new house needs new furniture
- Do you really have a contagious disease?
- Are you just convincing yourself it’s just a sinus infection?

So Who Can Get Me

- Honestly, more people than you think. A patient or employee COULD file a complaint against you with CDC or OSHA – both really bad things
- And remember show and tell?

This is not to be fooled with. If you have a contagious disease that could be communicated to another person through the normal activity of your business, stay home till you are well

Thank you for your attention and have a great 2015

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