Optometric Potpourri
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Disclosures
- Allergan Pharmaceuticals Speaker’s Bureau
- Bio-Tissue
- BioDLogics, LLC
- Katena/IOP
- Seed Biotech
- Johnson and Johnson Vision Care, Inc.

Definition
- Potpourri
  - A miscellaneous collection, a mixture of things

Definition

Ocular Emergency
- Immediate threats to the visual system that can lead to permanent loss of visual function if left untreated

Urgency vs. Emergency?
Levels of Urgency

- Immediate: within one to two hours
- Urgent: within 24 hours
- Semi-urgent: within a week
- Routine: within three to six months

Ocular Emergency?

- Chemical Burn? ☑
- Loss of vision? ☑
- Flashes/Floaters? ☑
- Itching? ☐
- Redness? ☒
- Tearing? ☐
- Discharge? ☐

Chemical Burn

Level of Urgency

- URGENT!!
- True Ocular Emergency

Chemical Injuries of the Cornea

- Acid: low pH
- Alkali: high pH
- Irritant: neutral pH
- Surfactants – detergents – neither acid or alkali
  - Cationic, anionic, nonionic
  - BAK
  - Liquid dishwashing detergent

Modifying factors

- Duration of contact
- Solution pH
- Solution quantity
- Solution penetrability

Acid Burns

- Intact corneal epithelium affords moderate protection against penetration of dilute or weak acids
  - Little damage seen unless pH < 2.5
  - Acids bind to corneal proteins and act as chemical barrier
  - Severe damage if epithelium removed
  - Cause protein coagulation in corneal epithelium
    - Also acts as barrier
    - Ground glass appearance
    - Usually non-progressive and superficial
    - Hydrofluoric acid is exception
      - Fluoride ion penetrates stroma
      - Acts as alkali

- Low pH
  - Sulfuric acid
  - Sulfurous acid
  - Hydrochloric acid
  - Nitric acid
  - Acetic acid
  - chromic acid
  - Hydrofluoric acid

- Rates of penetration
  - Sulfuric Acid - slowest
  - Hydrochloric acid - fast
  - Sulfurous acid – faster
  - Hydrofluoric acid - fastest
Substances that have basic (high) pH
More severe than acid burns
- As pH rises, emulsification of lipids in cell membranes occur
  - Destroying barriers to penetration facilitating deeper penetration to anterior segment
- Injurious effect on stroma involves:
  - Rapid destruction of corneal mucoproteins
  - Resultant stromal haze
  - Increasing as the pH is raised above 11.5
- Penetrate more rapidly than acids
  - Detectable levels in anterior chamber in seconds to minutes

**Calcium Hydroxide** Ca(OH)$_2$ (Lime)
- Found in plaster

*Sodium hydroxide* NaOH (Lye)
- Found in drain cleaners

*Ammonium hydroxide* NH$_3$ (ammonia)
- Found in household cleaners

Potassium hydroxide KOH (Caustic Potash)

Magnesium hydroxide Mg(OH)$_2$
- Fireworks - Combined chemical and thermal injury

**Calcium hydroxide** Ca(OH)$_2$ (Lime)
- Most common

*Sodium hydroxide* NaOH (Lye)
- Most serious

- Penetrates immediately into anterior segment structures

Irrigation
- Tetracaine
- Lid speculum
- Physiological saline
- Tap water

Instruct patient to irrigate with any type of water they have access to
- Eye wash
- Sink
- Garden hose
- Shower

**Goal**: 7.0 to 7.2

Check every 15-30 minutes
- pH testing OU, even if claims only one eye affected
- Trapped particles will cause pH change after initial normalization
- Special attention to fornix

Must neutralize pH first

- Involves corneal epithelium only
- Cornea remains clear
  - Epithelium denuded

Prognosis: Excellent for full recovery of normal corneal appearance and function
Cornea is hazy, but anterior segment structures are visible

Prognosis: Good

Concerns:
- Persistent epithelial dysfunction
- Conjunctivalization
- Haze
- Neovascularization

Stromal haze limits visualization of iris and lens

Prognosis: Guarded

Surgery needed for visual rehabilitation

Complete loss of corneal epithelium

Loss of proximal conjunctival epithelium

Opaque cornea

- No view of iris or pupil
- Ischemic necrosis of proximal conjunctiva and sclera

Prognosis: Extremely poor

- High risk for sterile ulceration and corneal melt

Macular Holes

Macular Degeneration

Cystoid Macular Edema

Diabetic Macular Edema

Central Serous Retinopathy

Retinal Nerve Fiber Layer (Glaucoma)

Anterior Segment?
Optical Coherence Tomography

- Essential tool for non-invasive analysis of retinal tissue for diagnosis and management of retinal disease and glaucoma.
- First reported in 1991 by Huang et al.
- Provides micron-scale cross sectional images of retina and choroid.
- Analogous to B-scan ultrasonography but uses light waves instead of sound waves.
- Near infrared light waves (800nm) prevents the need for contact with the globe.
- Resolution far exceeds that which can be achieve with ultrasound, computed tomography, or MRI.
- Great for patient education.
- Allows for quantification and comparison to norms.
- Can monitor progression or resolution of disease.

Optical Coherence Tomography

- Time domain 1996-2002
  - Compares a reflected beam of light to a beam of light from a reference center.
  - 400 A-scans/sec & 1 B-scan/1.6 sec.
  - Resolution 10um.
- Spectral Domain
  - Measures difference in wavelength between light from fixed reference that returns to tissue.
  - 27,000 A-scans/sec and 512 B-scans.
  - Resolution 5um.
- Spectral Domain provides more detailed images and more data with improved speed and accuracy.

Normal

- First interface encountered is between the transparent vitreous and reflective NFL.
- Deepest layer identified is RPE and choriocapillairs.
- Between the two is neuro-sensory retina.

Macular Holes

- Stage 1
  - Consists of a foveal detachment either with or without a full thickness defect.
  - Patients report sudden onset metamorphopsia.
- Stage 2
  - Associated with a full thickness defect that can be small or large and can appear slightly eccentric.
- Stage 3
  - Demonstrate larger, complete foveal defect greater than 400um in diameter.
- Stage 4
  - Full thickness hole with complete PVD.

Normal
Cystoid Macular Edema

- Cystoid Macular Edema
  - Causes
    - Medication side effects
    - Trauma/injury
    - Diabetes
    - AMD
    - Cataract surgery

Cystoid Macular Edema

- Most common cause of decreased vision after cataract surgery
- Usually 4-12 weeks after cataract surgery
- Incidence?
- Higher risk patients?

Case Study

- 81 year old AA female
- Medical history: HTN
- Ocular history: unremarkable
- Uncomplicated cataract surgery
- Uncorrected VA @ 3 months: 20/20 OD, OS
- Returned two months later
  - BCVA 20/30 OD, 20/60 OS

Case Study

- 57 year old white female c/o decreased vision OD for a few weeks
- Medical Hx: Thyroid disease (Synthroid)
- Ocular Hx: DES/Lid Margin disease (Restasis)
- BCVA: 20/40 OD, 20/20 OS
- Differentials?
- What questions do we need to ask?
Central Serous Retinopathy
- Localized detachment of sensory retina from underlying pigment epithelium

Retinal Nerve Fiber Layer (Glaucoma)
- Collects impulses that start with the rods and cones
- Carries neural impulses to the optic disc
- Lack of function causes loss of visual acuity or scotoma
- Lack of function causes the loss of vision in glaucoma patients

Anterior Segment Capabilities
- Can measure corneal thickness
- Can evaluate depth of FB
OCT

- Allows us to manage diseases
  - Monitor progression
  - Monitor improvement

“These Are a Few of My Favorite Things”

Disposable Spray Caps

- Convert standard ophthalmic drop bottle to spray bottle
- 12/pack
- $19.95
- Sigma Pharmaceuticals

New Therapies in Ocular Surface Disease

Case Studies

KeratoConjunctivitis Sicca
Sandra, 75 years old
Medical Hx:
- HTN, Osteoporosis
Ocular History
- Successful cataract surgery 2012 OU
- Longstanding dry eye syndrome
Medications
- Lotrel
- Fosamax
- Restasis
- FreshKote as needed

Options?

Ophthalmic Exam
- Decreased TBUT
- Dense and diffuse SPK
- Patient very photophobic

Options?

Options?

Sutureless Amniotic Membranes
- Anatomy
- Options
- Case Studies

Autologous Serum Eye Drops
- Benefits
- Clinical Indications

What is the amniotic membrane
- Innermost layer of the placentas
- Thin but tough transparent pair of membranes, which hold a developing embryo (and later fetus) until shortly before birth.

- The primary function of the amniotic membrane is to protect the fetus from:
  1. Anti-inflammatory
  2. Anti-scarring
  3. Anti-angiogenic
What is the Amniotic membrane

- Amnion is avascular and a translucent membrane composed of an inner layer of epithelial cells which are planted on a basement membrane.
- Basement membrane is comprised of Collagen I, III, IV, V and VII, laminin and fibronectin.
  - Found in conjunctiva and cornea.

Mechanisms of Action

- Promotes Epithelialization
- Suppresses Inflammation
- Inhibits Scarring
- Inhibits Angiogenesis
- Neurotrophic Factors
- Anti-Microbial Agent

All without the harmful side effects found in topical and oral medications.

Indications

- Acute Chemical/Thermal Burns
- Recurrent Corneal Erosions
- Neurotrophic Defects / Persistent Corneal Epithelial Defects
- Filamentary Keratitis
- Vernal Keratoconjunctivitis
- Recalcitrant Dry Eye
- Microbial Keratitis
- Nodular Degeneration
- PRK

Recurrent Corneal Erosion

- Chronic relapsing disease of corneal epithelium.
- Characterized by disturbance of epithelial basement membrane:
  - Defective adhesions
  - Recurrent breakdown of corneal epithelium
    - Redness, photophobia, tearing
    - Usually at night or upon awakening
    - May be related to REM during sleep
- Matrix metalloproteinase (MMP):
  - Name for group of enzymes that break down the structure of the extracellular matrix (collagenase)
- Elevated levels of MMP-9 and MMP-2 have been observed in tears of patients with RCE.

Recurrent Corneal Erosions

Pathophysiology

- Faulty BM with poor adhesion complexes
  - Poor epithelialization
- Increased MMP

AM Mech of Action

- Promotes Epithelialization
- Suppresses Inflammation
- Inhibits Scarring
- Inhibits Angiogenesis
- Neurotrophic Factors
- Anti-Microbial Agent

Courtesy of Ramamurthi et al.
**Clinical findings**
- Tear film instability
- Ocular inflammation
- Pro-inflammatory cytokines are upregulated
- Elevated levels of MMP noted

Sutureless amniotic membranes contain anti-inflammatory mediators, growth factors and cytokines
- Help restore a healthy and non-inflamed ocular surface
- Maintain a stable tear film

**Pathophysiology**
- Elevated Pro-inflammatory cytokines
- Elevated levels of MMP

AM Mech of Action
- Promotes Epithelialization
- Suppresses Inflammation
- Inhibits Scarring
- Inhibits Angiogenesis
- Neurotrophic Factors
- Anti-Microbial Agent

**Procurement**
- Membranes are procured and processed according to standards established by American Association of Tissue Banks (AATB) and FDA
- All recovered under full informed consent
  - From Caesarean vs. vaginal
- A thorough medical and social history of donor is obtained. Screened for:
  - HIV-1
  - HIV-2
  - HIV type 1 Nucleic Acid Test
  - HTLV-1
  - HTLV-2
  - Syphilis RPR
  - CMV
  - Hep B Core antibody
  - Hep C Antibody
  - Hep C Virus Nucleic Acid test

An absolute guarantee of tissue safety is not possible. Allograft has the potential to transmit infections disease to the recipient and the patient should be made aware
- Keep track of tissue used and lot numbers
- All data on file in regard to testing for the tissue
- Do Not use:
  - Areas with active or latent infection
  - Disorder that would create unacceptable risk of post op complications
  - Not to be used in eyes with GLC drainage devices or blebs

**Available Sutureless Membranes**

**Cryopreserved Amniotic Membranes**
Cryopreserved
Store in refrigerator x 3 months 1°C to 10°C (33.8°F to 50°F)
Store in freezer
- 1 year between -49°C to 0°C (-56.2°F to 32°F)
- 2 years between -85°C to -50°C (-121°F to -58°F)
Shelf life is 2 years from date of manufacturer
Allow to thaw to room temperature unopened for 5-10 min
Open inner pouch and remove using blunt forceps
Rinse with saline to reduce stinging sensation
Do not leave in eye longer than 30 days
Dehydrated Amniotic Membranes

- All stored at room temperature
- Shelf life typically 2-5 years
- Do not need to be rehydrated
- All require the use of BCL

Alpha Patch (Optix LLC)
AmbioDisk (IOP Inc. / Katena)
Aril (Seed Biotech)
BioDOptix (BioDLogics)
Oculomatrix (Skye Biologics)

Dehydrated Membranes

- Ambio Disk
  - Ambio 2 (35μ)
  - 9 or 15 mm
  - Ambio 5 (100μ)
  - Comes with a Kontur Precision Spherical CL
    - 8.9 bc
    - 16mm*, 18mm or 20mm

- BioDOptix
  - Two Disc Sizes
    - 12mm or 15mm
  - BCL of choice
  - Careful with sizing
  - 40-60μm thick membrane
**Dehydrated Membranes**

- **Aril**
  - 8 mm disc
  - 15 mm disc
  - 2 cm x 3 cm ellipse
  - 3 cm x 5 cm ellipse
  - 3 cm x 7 cm ellipse

- **VisiDisc**
  - 10 mm disc
  - VisiDisc Thin (45 microns)
  - VisiDisc Thick (200 microns)

**Thought to maintain growth and healing factors**

Not disrupted as may be the case in other dehydrated membranes

Used currently in wound care

Extending into ophthalmic setting

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**Case Study - CM**

- 62 year old female with DES x 7 years

Medical history significant for:
- HTN, hyperlipidemia, anxiety, PTSD, arthritis, osteoporosis, anemia, hypothyroidism, GERD

Ocular history significant for:
- Ocular surface disease

Medications:
- Synthroid, Elavil, Prilosec, Seroquil, Zocor, Atenolol, Klonopin, Neurontin

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**Complete the donor and recipient information form and return immediately**

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**Case Study - CM**

- Clinical exam
  - Decreased TBUT OU
  - Lissamine green and NaFl stain

Unable to continue Restasis

Decided on amniotic membrane
Clinical exam
- Removed ring at 1 week
- Improved corneal appearance
- Patient reported improved comfort

Continue artificial tears
- Long term options reviewed

Case Study - CM

- Clinical exam
- Removed ring at 1 week
- Improved corneal appearance
- Patient reported improved comfort

Recurrent Corneal Erosion

WR, 50 year old male
Initial visit August 2011
Presented with c/o foreign body/irritation OD
Medical Hx: HTN, hyperlipidemia
Ocular Hx: Unremarkable

Recurrent Corneal Erosion

- Clinical Exam (September 2012)
  - BCVA 20/20 OD, OS
  - Slit lamp exam
    - Blepharitis/Meibomitis
    - DFE
      - Unremarkable

- Clinical Exam (July 2013)
  - Presents with c/o symptoms of RCE OD
  - Cornea clear OD/OS
  - Treatment: Start Muro 128 ointment QHS OD

Case Study

- Clinical Exam (August 2013)
  - Patient more symptomatic
  - Change treatment course

Case Study

- Clinical Exam (August 2013)
  - Patient more symptomatic
  - Change treatment course
  - Debrided cornea OD
  - BCL x 2 months
  - Add Azasite BID
  - Less symptomatic until January 2014
Clinical Exam (March 2014)
- New Plan

Debrided cornea

Debrided cornea

ProKera Slim AM inserted

Doxycycline 20 mg BID x 2 months
Lotemax gel TID OD x 1 month

Clinical Exam (April 2014)

Debrided cornea

Autologous Serum

- Use first described in 1984 by Fox et al (for keratoconjunctivitis sicca)


- DEWS / ITF - Severity Level 3 Treatment

- Unpreserved, non-antigenic

- Utilizes patients own blood serum

- Blood is drawn and serum is spun down and mixed with artificial tears / 0.9% sodium chloride

- Doesn’t contain red blood cells and clot factors
**Autologous Serum**

- Contains essential components in tears
  - epidermal growth factor
  - hepatocyte growth factor
  - fibronectin
  - neurotrophic growth factor
  - vitamin A

- Potential complications
  - Immunoglobulin deposits
  - Corneal infiltrates
  - Conjunctivitis
  - Decreased corneal sensitivity

**Concerns:**
- Costly - $150-300 time, 2-4x/year
  - Typically not covered by insurance
- Inconvenient - Requires blood donation from patient
- Need to store frozen for up to three months at −20°C
- Keep away from light to avoid degradation of Vitamin A
- Possible risk of infection
  - Cornea and systemic

**Compounding Pharmacy**

Physician's Compounding Pharmacy
1900 S. Telegraph Road, Suite 102
Bloomfield Hills, MI 48302
Phone: 248-758-9100
Fax: 248-758-1831

**Newer Technologies**

- Disease-specific, tailored drug release and plug persistence
- Easy to insert, familiar procedure to physicians
- Non-invasive
- Absorbable – no need for removal
- Allows for visualization by the patient and the physician

**Anterior Segment Therapies**

- Fluorescent plug observed under blue light
- Product Design

- Procedure
  - Easy to insert, familiar procedure to physicians
  - Non-invasive
  - Absorbable – no need for removal
  - Allows for visualization by the patient and the physician

*Courtesy of Dublin Therapeutics*
**Value Proposition**
- Strong steroid, soft delivery
- 1x administration replaces 4x/day dosing over a week period
- Plug tailors release with tapered administration for 30 days
- 7% of the drop equivalent dose; no IOP spikes observed in Phase 2

**Plug Characteristics**
- Easy to insert
- Comfortable for the patient
- Absorbable – no need for removal

**Status**
- Phase 3 trials complete for post-op inflammation and pain
- Topline results reported for Phase 2 trial for allergic conjunctivitis

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**New Technologies and Ideas are Great**

Most of the time.....

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**Thank you**

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