Amniotic Membrane Workshop

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Advanced Recalcitrant PEK In Ocular Surface Disease

- Androgen drops
- Amniotic Membrane
- Anti-inflammatory
  - Topical
  - Systemic
- Autologous Serum
- Intense pulse light therapy
- MGD therapies (Lipiflow, Miboflo, manual)
- Punctal occlusion
- Tetracycline

Amniotic Membranes

What is Human Amniotic Membrane?

- A unique, avascular membrane separating the mother from the fetus: inner lining of placenta
- Provides an incubating environment promoting cellular differentiation
- Provides an immunological barrier to prevent "foreign body" rejection

Amniotic Membrane - Profile

- Unique Grafting Characteristics
  - Provides a matrix for cell migration/proliferation
  - Natural biological barrier
  - Non-immunogenic
  - Stores at room temperature
  - Mimics the profile of conjunctiva

What is Human Amniotic Membrane?

- Studies show amniotic membrane enhances the wound healing process:
  - It reduces pain
  - It reduces inflammation
  - It reduces scar formation
  - Contains essential growth factors for cell growth and diversification
Clinical Challenges in Ocular Surface Disease

- **DEFECT**
- **DELAYED HEALING**
- **DYSTROPHY**
- **DEGENERATION**
- **DAMAGE**

Sutureless Amniotic Membranes

- Used to manage ocular surface healing for a variety of indications including:
  - Corneal epithelial defects
  - High-risk corneal transplants
  - Recurrent Corneal Erosion
  - Infectious Diseases (Herpes/Keratitis)
  - Stevens-Johnson Syndrome & Chemical Burns

Sutureless Amniotic Membranes

- Chemical Burns
- Mechanical Complications secondary to graft
- Disruption of surgical wound
- Non-healing surgical wound

Biological Scaffolding

- Helps initiate an active healing process by providing proteoglycans and growth factors
- Collagens, fibronectin and laminin
- Cryopreserved membrane contains heavy-chain hyaluronic acid
- Inhibits proinflammatory cells
- Suppress T Cells

Technology Highlights

Impressive regenerative platform that possesses natural growth factors and optimal scaffolding properties within a complex extracellular matrix that are:
- Anti-inflammatory
- Anti-scarring
- Anti-angiogenic

Therapeutic actions:
- Promotes Stem Cell Expansion
- Suppresses pain
- Promotes cellular migration
- Expedites recovery

Inflammation is the Hallmark of All Ocular Surface Diseases

- Ocular Surface Disease
  - Corneal Inflammation
  - Conjunctival Inflammation
  - Eyelid Inflammation

  - Keratitis
  - Conjunctivitis
  - Blepharitis
Normal Adult Wound Healing

Our body does not achieve state-of-the-art healing on its own…

- PROLONGED INFLAMMATION
- RESIDUAL HAZE
- SCAR FORMATION

**Inflammation’s Effect on Healing**

- Inflammation: the first sign of wound healing & is also the hallmark symptom of all ocular surface diseases
- Uncontrolled inflammation leads to:
  - Chronic pain and discomfort/irritation
  - Delayed healing, more tissue damage
  - Vision-threatening complication, e.g., scar/haze
- Effective control of inflammation is an important strategy to promote healing and minimize the risk of scar/haze

**Controlling Inflammation is Key to Preventing Tissue Damage!**

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**Diabetic Foot Ulcer**

**DIAGNOSIS & PATIENT HISTORY**

Patient suffering from a chronic diabetic wound open for 5 years, failed serial debridement, wound vacs, and allografts. Now the patient has formed a contralateral ulcer.

**NEOX® TREATMENT & OUTCOME**

Patient brought to the OR for sharp debridement and first NEOX® application. Second and third NEOX® applications placed in the first 4 weeks with both wounds nearly healed to date (10 weeks).

**Chemical Burn**

**Difference Between Cryopreserved and Dehydrated Amniotic Tissue**

**HC-HA/PTX3 Orchestrates the Regenerative Healing Process**

*By Modulating the Innate and Adaptive Immune Response*

- Facilitates Neutrophil Apoptosis (Cell Death)
- Changes M1 Inflammatory Macrophages to M2 Anti-Inflammatory Macrophages
- Suppresses Th1 & Th17 Lymphocyte Activation
- Promotes Regenerative Healing
Scarless Fetal Wound Healing

Speed & Quality of Healing Count!

Giant neck mass resection at 26 weeks in-utero

3 months

HC-HA/PTX3, found naturally in amniotic membrane, is the critical biologic component responsible for scarless fetal wound healing.

The processing method is the key to retaining potency.

CRYOTEK® cryopreservation method allows us to preserve AM at -80°C without forming ice (minimal manipulation from fresh AM). Thus, our products:
1. Maintain the structural and biological integrity of the membrane
2. Retain meaningful quantities of HC-HA/PTX3 to activate regenerative healing
3. Retain the original tensile strength of AM, facilitating ease of handling during surgery

PROKERA® utilizes the proprietary CryoTek™ cryopreservation process that maintains the active extracellular matrix of the amniotic membrane which uniquely allows for regenerative healing.

PROKERA® is the only FDA-cleared therapeutic device that both reduces inflammation and promotes scar less healing

PROKERA® can be used for a wide number of ocular surface diseases with severity ranging from mild, moderate, to severe

The Prokera Slim, Regular, Plus

Insertion of Cryopreserved Amniotic Tissue

• Open package exposing contained membrane
• Rinse with saline liberally
• Apply topical anesthesia
• Hold upper lid and have patient look down
• Insert into superior fornix
• Slide under lower eyelid
• Check for centration

Contraindications
• Not to be used with patients with glaucoma filters
• Allergies to Ciprofloxacin or Amphotericin B

The processing method is the key to retaining potency.
**Post-Treatment Protocol**

- **Continue medications**
- **Apply Temporary Tarsorrhaphy (PRN)**
  - Tape
  - Tegaderm
  - “Breathe-Right” nasal strips

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**Tape Tarsorrhaphy**

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**PROKERA® Removal**

- Topical Anesthetic
- Pull the lower eyelid
- Lift the lower edge of PROKERA® using a Q-tip or forceps
- Ask the patient to look down
- Slide the PROKERA® out with gentle pressure on the upper eyelid

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**Dehydrated Amniotic Membranes**

- BioDOptix (BioD LLC)
- Aril (Seed Biotech)
- Oculomatrix (Skye Biologics)
- AmnioOcular (Liventa BioScience)
- Alpha Patch (Optix LLC)
- AmbioDisk (IOP/Mimedix)

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**Dehydrated Amniotic Membrane Products**

- All store at room temperature
- Shelf Life typically 2-5 years
- Do not need to be rehydrated
- All require the use of BCL
AmbioDisk
Amniotic Membrane Technology
• Purion® Preservations Process
• Dehydrated
• Terminally sterilized
• Retained biostructure
• Over 75,000 surgeries

BioD
Amniotic Membrane Technology
• DryFlex® processing technology
• Dehydrated
• Retains growth factors, cytokines and collagens
• Sizes – 9.0mm / 12.0mm

• Patient in supine position
• Speculum the eyelids
• Apply topical anesthesia

• Maintain dry ocular surface
• Center graft on cornea
• Gently smooth using traction, counter traction
• 1-2 mm over peripheral conj
• Disregard small creases and bubbles
• “IOP” oriented facing downward

• Apply appropriately sized BCL
• Center lens over AmbioDisk
• Maintain centration of amniotic disk over cornea

• Gently remove speculum
• Request several blinks
• Disregard small bubbles, creases
• Apply appropriate meds
• < 10 minute procedure
Follow up: Variable
- Dissolves during healing
- Absorption: 7-10 days
- Rx: OD discretion, judgment

Common Corneal Pathologies Associated with Dry Eye
- Superficial Punctate Keratitis
- Filamentary Keratitis
- Recurrent Corneal Erosion
- Corneal Ulcers
- Neurotrophic Keratitis
- Exposure Keratitis
- Sjogren’s Syndrome

Offer Something New
- **TREAT THE CORnea with PROKERA®**
  - Anti-inflammatory, anti-scarring actions
  - Nerve growth factors
  - Hydrated environment that boosts stem cell proliferation

- **What this means for your dry eye patients**
  - Highly effective with extended periods of relief (average of 6 symptom-reduced/free months)
  - Rapid treatment period: 4-7 days
  - Crystal clear cornea
  - See and feel better
  - Happy eyes, happy patients!

Patient Survey Evaluates the Effectiveness of PROKERA® Slim in Treating Dry Eye

Patient Survey Results
- **95%** of respondents said they would recommend PROKERA® Slim to a non-treatment friend
- **95% of respondents said they felt better**
- **81%** of respondents said PROKERA® Slim was comfortable during treatment

Patient Enrollment
As of April, 2014, over 560 patients have enrolled in the study with 160 respondents, of which 108 (68%) are females and 52 (32%) are males with over half of the respondents were 50 years of age or older. Of the respondents to date, 75% have been suffering from dry eye for three years or more, and 80% currently use or have used eye drops in the past 30 days.

**Case Study**
- **72 YOAAF** – Referred by OD for Cataract Eval OU. Blurred VA. Occasionally uses ATs prn.
- Med Hx of allergies, acid reflux and HTN
- SLE: 3+ NS OU
- Uneventful cataract sx OU
  - OD 1/4/12  OS 2/1/12

**Case Study**
- **3/27/12** Increased light sensitivity / pain OU
  - Dx: Rebound Iritis OU
  - Tx: Restart difluprednate and nepafenac TID OU

- **5/14/12** F/u chronic iritis OU, FBS OS
  - Dx: Improved Chronic Iritis OU, Dry eye disease OS>OD
  - Tx: Decrease steroid and NSAID to BID OU, ATs BID OU
Case Study

- 9/7/12 – F/u chronic iritis, FBS OS>OD, Tearing
  - Dx: Resolved iritis OU, Dry eye disease OU
  - Tx: Start on cyclosporine 0.05% OU, F/u 4-6 mos

- 2/25/13 – F/U dry eye disease OU, OS always has a FBS, Chronic tearing
  - Dx: DED OU / See photo
  - TearLab: 298 / 301

Conjunctival Chalasis (CCH)

- Breakdown of Tenons Capsule
- MMP 9
- Fibro vascular gel like tissue

Referred to Conjunctival Resection

- Dx: Conjunctival chalasia OS>OD
- Tx: Schedule for conjunctivoplasty OS
  - Disc R/B/A to surgery including 50% chance that symptoms will not improve even after a successful operation.
  - Pt elected to proceed with conjunctivoplasty OS only, as that is the more symptomatic eye.

Definition of Reservoir Restoration Procedure (n): A simple, surgical procedure for Conjunctivochalasis Dry Eye that restores the function of the anatomical tear reservoir (fornix) by:
1) Removing deteriorated Tenon’s Capsule
2) Rearranging or removing loose conjunctiva
3) Deepening the fornix, and
4) Using cryopreserved amniotic membrane to replace the Tenon’s and conjunctiva, to help prevent recurrence, and to expedite a patient’s recovery.
CCh Also Obstructs the Tear Meniscus and Blocks Tear Clearance

CCh interferes with the tear meniscus
Surgus et al. AJO. 2010; 138:734-96

CCh blocks tear flow into the punctum to cause delayed tear clearance

Go to the Source:
Hydrodynamics (Water Movement) that Hydrates the Ocular Surface

1. FORNIX
2. MENISCUS
3. OCULAR SURFACE

CCh Paradox:
Why are some CCh patients asymptomatic?

Normal
CCh without Symptoms
CCh with Symptoms
CCh after AMT

Blinking helps ATD dry eye, but not CCh dry eye
Di Pascuale et al. BJO. 2004;88:388–392

Why not just cut it off or cauterize it?
Scar Formation, Fat Prolapse, and not Correcting the Fornix

The Surgical Minute
Review of Optometry

Reservoir Restoration using AmnioGraft®
PRE OP
5 YEARS POST OP
Self Retaining Amniotic Membrane

- Cost of ProKera Approximately $900 to $1000
- Cost of AmbioDisc / Bio Optix Approximately $600
- Medicare Allowable Virginia $1400***

Overcoming Objections

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<tr>
<th>Objections</th>
<th>Response</th>
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<tr>
<td>Lack of perceived clinical value</td>
<td>Peer reviewed journal articles and case studies</td>
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<td>Perceived inferiority to a competitor/product</td>
<td>Competitively priced with superior handling characteristics, performance</td>
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<tr>
<td>Too expensive</td>
<td>Explore how we can break in, whether by price or other means</td>
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<tr>
<td>Initiative with another group</td>
<td>Case studies, key thought leaders, peer reviewed journal articles</td>
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<td>Clinical proof</td>
<td>New packaging with excellent feedback from clinicians</td>
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<td>Packaging</td>
<td>BioDOptix is reimbursed with the same codes and same manner as the competitive tissue</td>
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<tr>
<td>Patent issues</td>
<td>IOP has no patent that precludes BioD from distribution of BioDOptix tissue</td>
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Wetlab

- Gloves
- Saline Solution
- Remove Protective Covering
- Retention Ring
- Rinse with Retaining Ring in Place
- Remove ProKera
- Rinse in Gloved Hand
- Determine Right Side Up

Thank You!!

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