Amniotic Membrane

Regenerative Matrix Therapy

Feel Comfortable with Amniotic Membranes in One Hour

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Optometric Education Consultants
February 16, 2017

Disclosure Statement
(next slide)

Disclosures- Greg Caldwell, OD, FAAO

- Will mention many products, instruments and companies during our discussion
  - I don't have any financial interest in any of these products, instruments or companies
- Pennsylvania Optometric Association –President 2010
  - POA Board of Directors 2006-2011
- American Optometric Association, Trustee 2013-2016
  - Thank you to the members and those who join
- I never used or will use my volunteer positions to further my lecturing career
- Lectured for: Shire, BioTissue, Optovue
- Advisory Board: Allergan
- Envolve: PA Medical Director, Credential Committee

Course Description and Learning Objectives

In office and sutureless amniotic membrane (AM) is emerging as an excellent alternative due to promising clinical outcomes to treat a variety of ocular surface conditions rapidly and effectively. This course will review what is an amniotic membrane, the various types of AMs, clinical applications, patient experience, insertion, and removal.

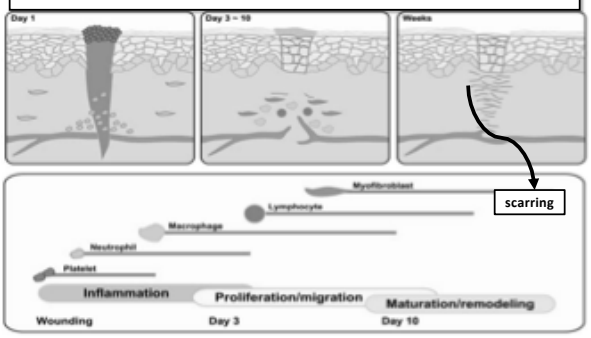
- Review an amniotic member and the beneficial properties
- Review the types of amniotic membranes available for ocular usage
- Identify ocular conditions appropriate for an amniotic membrane
- Review patient experience
- Review insertion and expectations
- Review removal of ring when indicated

Amniotic Membrane History

- Amniotic membrane transplantation (AMT) in ophthalmic surgery
  - First documented in 1940
- 1995 Kim and Tseng used AMT for ocular surface reconstruction
- 1997 AmnioGraft (BioTissue), first in USA
  - Surgical AMT, sutured
- 2005 ProKera (BioTissue), single sheet, self retained, polycarbonate, in-office and sutureless
- 2012 AmbioDisk (Katena/IOP), sutureless
- 2013 BioD Optix (BioD), sutureless

Adult Wound Healing

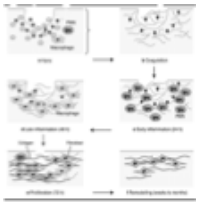
Insight into the Relationship between "Inflammation" and "Regeneration"

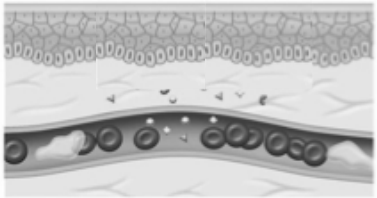


Shaw et al, *Endocrine, Metabolic & Immune Disorders - Drug Targets*, 10:320-330, 2010

Regeneration vs. Repair

- Regeneration = cells/tissue reproduction = NO SCAR
- Repair= Healing by granulation tissue / scar formation
  - Scarring correlates directly with Inflammation
  - Controlling Inflammation → Reduces Scarring



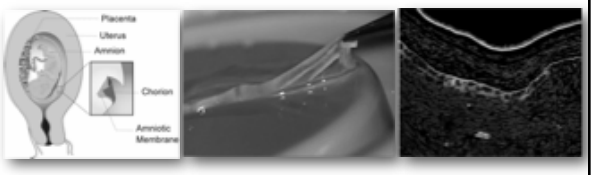


Amniotic Membrane
Regenerative Wound Healing

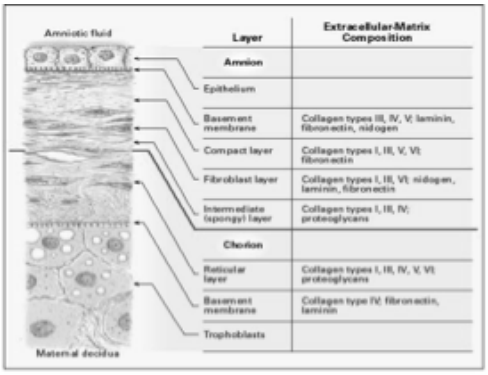
- Amniotic membrane shares the same cell origin as the fetus
  - Stem Cell behavior
- Structural similarity to all human tissue
  - Tissue replacement/ Less granulation
- Regenerative tissue response away from:
  - Inflammation
  - Angiogenesis
  - Scarring
  - Rejection

The Amniotic Membrane

- The amniotic membrane is the innermost lining of the placenta (amnion)



Structure of the Fetal Membrane

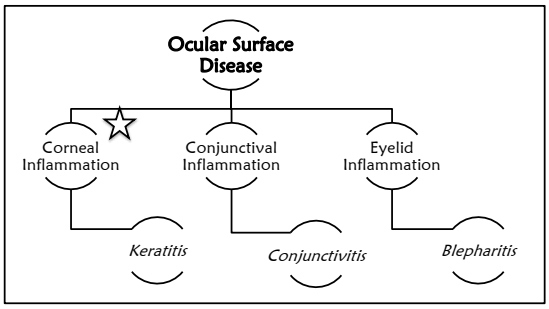


Layer	Extracellular-Matrix Composition
Amnion	
Epithelium	
Basement membrane	Collagen types III, IV, V; laminin, fibronectin, nidogen
Compact layer	Collagen types I, III, V, VI; fibronectin
Fibroblast layer	Collagen types I, III, VI; nidogen, laminin, fibronectin
Intermediate (spongy) layer	Collagen types I, III, IV; proteoglycans
Chorion	
Reticular layer	Collagen types I, III, IV, V, VI; proteoglycans
Basement membrane	Collagen type IV; fibronectin, laminin
Trophoblasts	

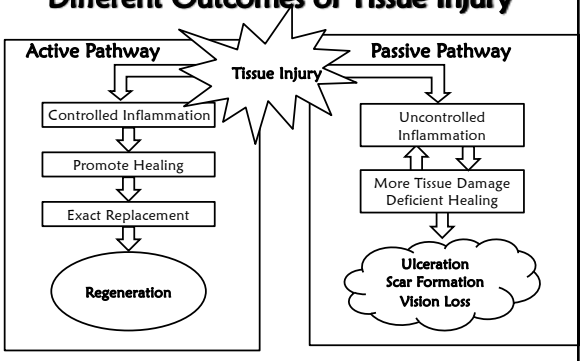
Regenerative Tissue Engineering

- Innovative biologic healing
- A 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



Different Outcomes of Tissue Injury



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Passive vs. Active Therapy

Passive is a single-action therapy that may reduce inflammation but may delay healing

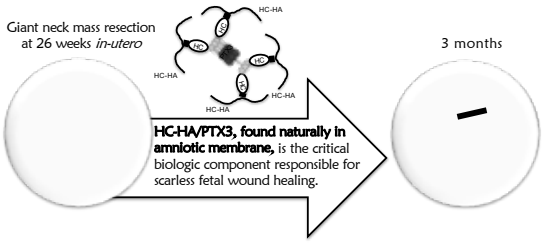
- Therapeutic Contact Lenses are a **Passive** Therapies
  - Provide mechanical protection
  - Potential to induce infection
- Steroids/ NSAIDs are **Passive** Therapies
  - Reduce inflammation
  - Delay healing
  - Potential to flare-up infection

Active is a dual action therapy that controls inflammation & promotes scarless healing

- Amniotic membranes are an **Active** Therapy (Biologic Corneal Bandage)
  - Controls inflammation
  - Prevents additional damage
  - Promotes and accelerates wound healing
  - Prevents / reduces scar formation

Scarless Fetal Wound Healing

Speed & Quality of Healing Count!



Courtesy of fetal surgeon, Michael Harrison, M.D. (UCSF)

Diabetic Foot Ulcer

Diagnosis & Patient History

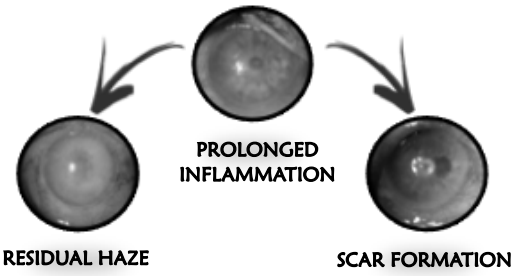
Patient suffering from a chronic diabetic wound open for 5 years; failed serial debridement, wound vacs, and allografts. Now the patient has formed a contralateral ulcer.

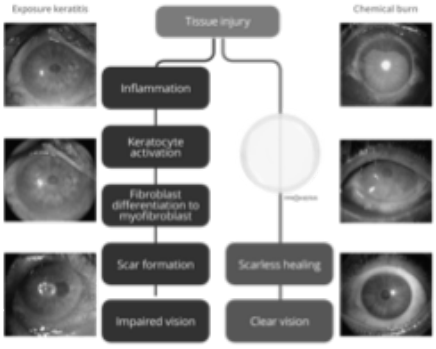
NEOX® Treatment & Outcome

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).

Normal Adult Wound Healing

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





Damage

Healing with Scar Formation	Healing without Scarring

Ocular Surface Disease Challenges

- Defect
- Delayed healing
- Dystrophy
- Degeneration
- Damage

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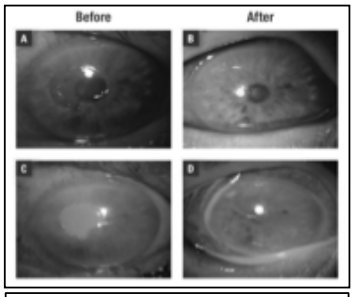
DEFECT

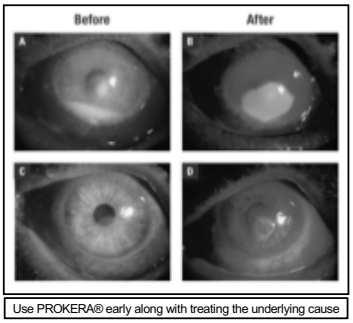
Neurotrophic Persistent Epithelial Defect



Use PROKERA® early along with treating the underlying cause

DEFECT

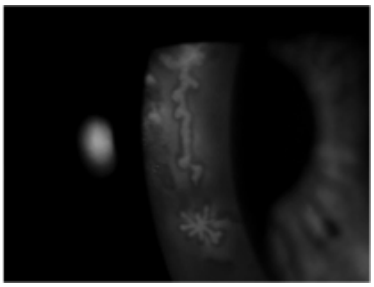
Infectious Keratitis: Corneal Ulcer with Hypopyon



Use PROKERA® early along with treating the underlying cause

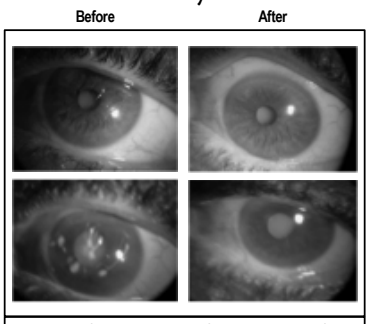
HSV

24-48 hours before Zirgan arrives



DELAYED HEALING

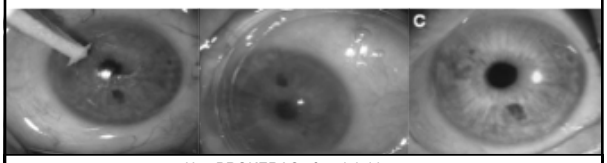
Filamentary Keratitis



Failure of standard therapy justifies concomitant use of PROKERA®

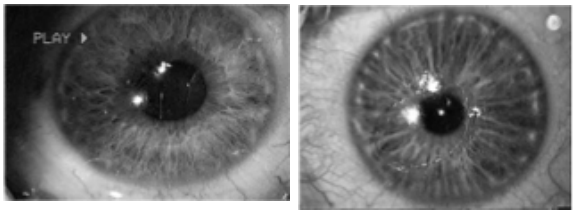
DYSTROPHY

Recurrent Corneal Erosion



Use PROKERA® after debridement

RCE



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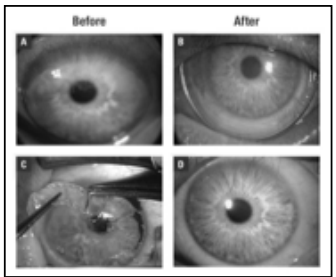
DEGENERATION

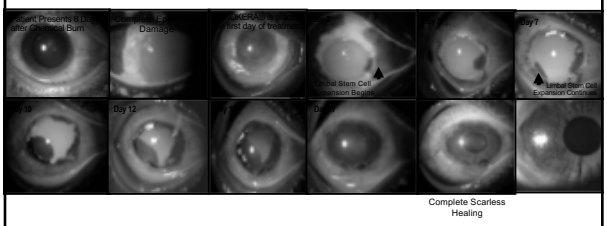
Salzmann's Nodular Degeneration



Use PROKERA® after superficial keratectomy

DAMAGE

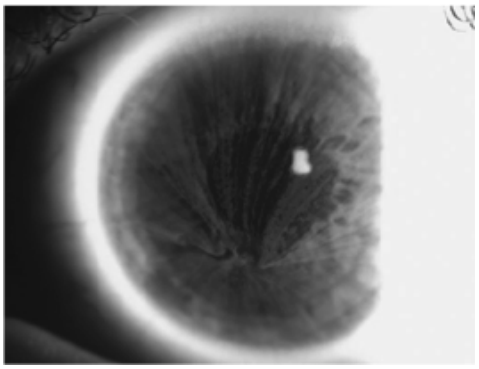
Chemical Burn



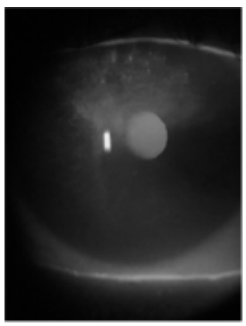
DEFECT, DELAYED WOUND HEALING, DAMAGE

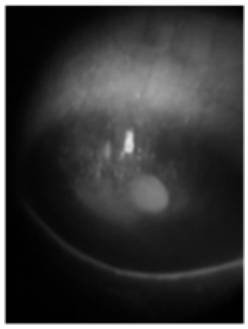
Stem Cell Burnout

Stem Cell Burnout



Limbal Cell Exhaustion





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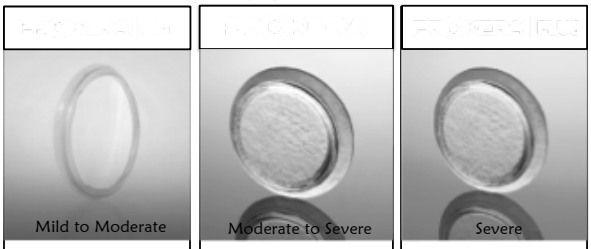
Ocular Surface Disorders and Defects
including but not limited to

- Any Persistent or Non-healing Epithelial Defect
- Corneal Erosions and Ulcers
- Corneal Scars and Opacities
- Keratoconjunctivitis Sicca
- Neurotrophic or Exposure Keratoconjuntivitis
- Acute Thermal and Chemical Burns
- Keratitis (Punctate, Filamentary, Dendritic, Photo-)
- Post-infectious Keratitis (Herpetic, Vernal or Bacterial)
- Band or Bullous Keratopathy
- Adjunctive Therapy for PRK
- Foreign Body Removal
- Conjunctival Defects
- Corneal Dystrophies, including Anterior Basement Membrane Dystrophy
- Stevens-Johnson Syndrome

Sutureless Amniotic Membrane
wound healing vs wound covering

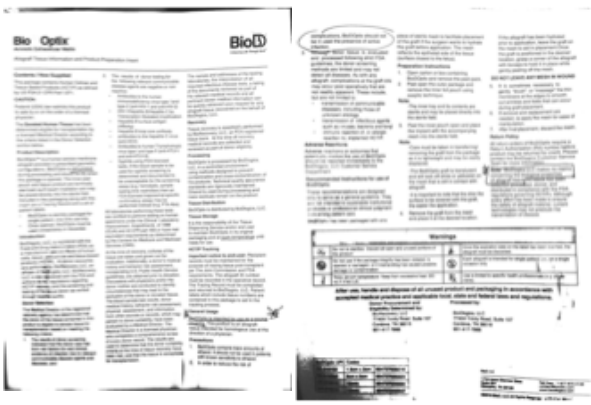
- Cryopreserved- wound healing
  - PROKERA- BioTissue
- Dehydrated- wound covering
  - AmbioDisk -IOP Ophthalmics- Ketena
    - Single layer, shiny/matte side
  - BioD – BioD Optix
    - Single layer, IOP for proper side
  - Aril- Seed Biotech/Blythe Medical
  - Eclipse- Ophthalogix
    - Single and dual layer
    - 45 microns of amnion, increased tensile strength

PROKERA®
Cryopreservation



Mild to Moderate	Moderate to Severe	Severe
Keratitis (Microbial, HSV) Recurrent Corneal Erosions Corneal Abrasions / Wounds	Neurotrophic PED Severe Infectious Keratitis Post DSEK for Bullous Keratopathy Corneal Wounds	Chemical Burns Stevens Johnson Syndrome Severe Corneal Ulcers Corneal Wounds

Dehydrated/Dry



The donor has been screened for the following infectious diseases

- HIV-1 & HIV-2 Antibody
- HIV-1 (RNA-NAT)
- Hepatitis B Surface Antigen (HBsAg)
- Hepatitis B Core Antibody (HBcAb)
- Hepatitis B Virus (HBV, DNA-NAT)
- Hepatitis C Antibody (HCVAb)
- Hepatitis C Virus (HCV, RNA-NAT)
- Syphilis (RPR)
- HTLV I & II Antibody (HTLV I/II Ab
- A blood specimen, drawn within ±7 days of donation
  - FDA or CMS guidelines
- Microbial testing has also been performed on the final product to identify
  - Aerobic
  - Anaerobic
  - Fungal

Amniotic Membrane Components

- Proteoglycans
- Growth factors
- Collagens (types I, III, IV, V and VI)
- Fibronectin
- Laminin
- Heavy chain hyaluronic acid (HC-HA)
- PTX 3 (HC-HA Complex)
  - Pentraxin 3

Direct inhibition of pro-inflammatory cells[11]
- Suppresses T-cell activation
- Inhibits giant cell formation
- Controls MMP production[7]

Cryopreservation vs. Dehydrated

The difference is clear

HC-HA/PTX3 Orchestrates the Regenerative Healing Process

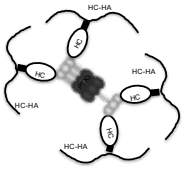
By Modulating the Innate and Adaptive Immune Response

Facilitates Neutrophil Apoptosis (Cell Death)

Changes M1 Inflammatory Macrophages to M2 Anti-Inflammatory Macrophages

Suppresses Th1 & Th17 Lymphocyte Activation

Promotes Regenerative Healing

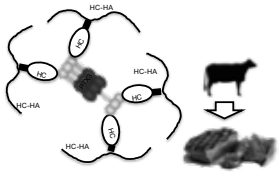


Understanding the Significance of the Processing Method

Many things start off the same…

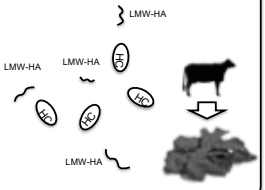
CryoTek ADVANTAGE

- Preserves meaningful quantities of all extracellular matrix components
  - Including HC-HA/PTX3



Dehydration

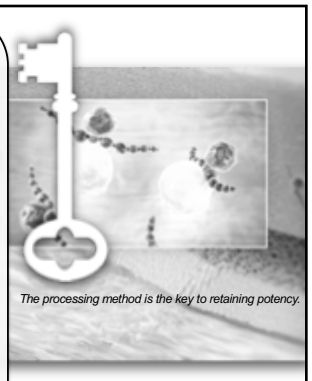
- Breaks down HC-HA/PTX3 to pro-inflammatory low molecular weight HA
- Structural integrity is lost.



CryoTek ADVANTAGE

CRYOTEK® Cryopreservation

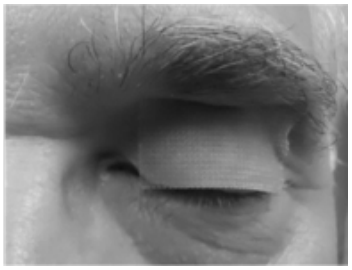
- Preserve AM at -80ºC
  - Without forming ice
  - Minimal manipulation from fresh AM
  - Maintains the structural and biological integrity of the membrane
  - Retains meaningful quantities of **HC-HA/PTX3**
    - Activate regenerative healing
  - Retain the original **tensile strength** of AM
    - Facilitating ease of handling during surgery



The processing method is the key to retaining potency.

Minor Surgery Consent Form Insertion

Taped tarsorrhaphy/tapesorrhaphy



CPT CODE 65778

Sutureless Placement of Amniotic Membrane on the Ocular Surface

2016 - National Medicare Reimbursement Rate: $1,448.00

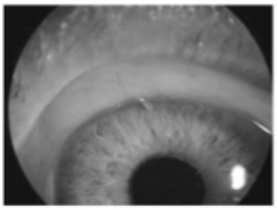
$1,575.87 Medicare in PA-01
$1,351.14 Medicare in PA-99
$1,629.28 Medicare in NJ-99

2017- $1338 Medicare (Michigan minus Detroit)

CPT Code 65778 has a 0-Day Global Period

Contraindication

- Drug reactions to Ciprofloxacin or Amphotericin B (ProKera)
- Eyes with glaucoma drainage devices or filtering bleb
- Incomplete blink or eyelid closure issues



Why Intervene with an Amniotic Membrane

- Achieve optimal corneal healing
  - Faster Re-Epithelialization
  - Intervention against Scar Formation
  - Improved Rates of Corneal Clarity
  - Consider wound healing catalyzed by PROKERA®'s CRYOTEK™ Platform Technology
- Intervene early in Ocular Surface Disease
  - Defect
  - Delayed Healing
  - Dystrophy
  - Degeneration
  - Damage

Questions

Thank-You and Hope You Enjoyed

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