Amniotic Membrane Regenerative Matrix Therapy
Feel Comfortable with Amniotic Membranes In One Hour

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Disclosure Statement (next slide)

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"

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

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

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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

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

Active Pathway
- Controlled Inflammation
- Promote Healing
- Exact Replacement
- Regeneration

Passive Pathway
- Uncontrolled Inflammation
- More Tissue Damage
- Deficient Healing
- Ulceration
- Scar Formation
- Vision Loss
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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 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

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Diabetic Foot Ulcer

**Diagnosis & Patient History**
Patient suffering from 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…

**Residual Haze**
**Scar Formation**

Ocular Surface Disease Challenges

- **Defect**
- **Delayed Healing**
- **Dystrophy**
- **Degeneration**
- **Damage**

Scarless Fetal Wound Healing

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

DELAYED HEALING
Filamentary Keratitis

Failure of standard therapy justifies concomitant use of PROKERA®.

DYSTROPHY
Recurrent Corneal Erosion

Use PROKERA® after debridement.

RCE
DEGENERATION
Salzmann’s Nodular Degeneration

DAMAGE
Chemical Burn

DEFECT, DELAYED WOUND HEALING, DAMAGE

Stem Cell Burnout

Limbal Cell Exhaustion
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 Szza
- Neurotrophic or Exposure Keratoconjunctivitis
- Acute Thermal and Chemical Burns
- Keratitis (Punctate, Filamentary, Dendritic, Photo-)
- Post-infectious Keratitis (Herpetic, Vernal or Bacterial)
- Band or Bullous Keratopathy
- Adjunctive Therapy for PPK
- 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

The donor has been screened for the following infectious diseases:

- HIV-1
- HIV-2
- HIV-1 (RNA-NAT)
- Hepatitis B Surface Antigen (HBsAg)
- Hepatitis B Core Antibody (anti-HBc)
- Hepatitis B Virus (HBV, DNA-NAT)
- Hepatitis C Antibody (anti-HCV)
- 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
* Microbiological 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

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

Cryopreservation vs. Dehydrated

The difference is clear

Understanding the Significance of the Processing Method

Many things start off the same...

CRYOTEK® Cryopreservation
- Preserve AM at -80°C
  - 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

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
$1,391.14 Medicare in PA-99
$1,629.28 Medicare in NJ-01
$1,351.14 Medicare in PA-99
$1,629.28 Medicare in NJ-99
2017- $1338 Medicare (Michigan minus Detroit)

0 DAYS
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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