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Amniotic Membranes In Primary Eye Care

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PCS · CodeSAFEPLUS · EyeCode Education

Peter J. Cass, OD - Disclosures



- Chief Technology Officer, **Practice Performance Partners**
- **Benedict Professor in Practice Management**, University of Houston College of Optometry
- Chairman of the Board, **Elevated Digital Optics** Lab
- Optometrist, MyEyeDr, Beaumont, Texas
- Past President, Texas Optometric Association
  - Chair TOA HIT Committee, Chair AOA Nominating Committee, TOA COVID-19 Taskforce, TOB COVID-19 Taskforce, Third Party committee, L&L committee, AOA HIE Workgroup,
- Consultant/Speaker for ophthalmic companies:
  - Alcon, Bausch & Lomb, Crystal PM, Diopsys, Optos, Solution Reach, Katena, Tear Science, Shire, BioD, Weave
- Lecturer for
  - Professional groups: Vision Source, Vision West, ECPN, PERC, Vision Trends, TSO, etc.
  - Universities: RSO, UAB, etc.
  - State associations: TOA, and over 20 others
- Shareholder EKKDA, EDO labs, PCS

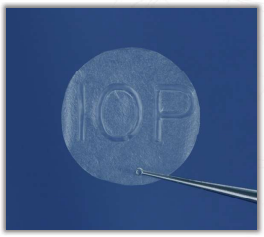
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Types of Disks Available

- Cryopreserved



- Dehydrated



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Cryopreserved Overview

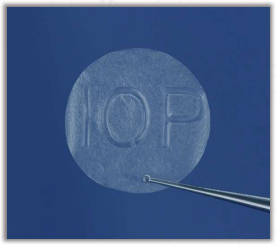
- Sizes
  - Inner diameter of 16mm
  - Outer diameter of 21 mm
  - Clipped to a **dual polycarbonate ring** system
- **10-minute Office Procedure**
- Must be stored at **freezing** temperature
- Can last up to **1 year**



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Dehydrated Overview

- Single layer of AM
  - 40 microns thick (nominal)
  - Sizes: 9mm/12mm/15mm
- With chorion layer
  - 100 microns thick (nominal)
  - Sizes: 15mm
- **Fixated with BCL**
- 10-minute Office Procedure
- Can be stored in **exam room drawer**
- Can last up to **5 years**

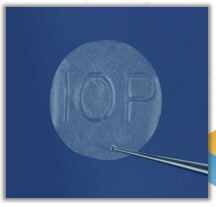


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Clinical Use

- **Cryopreserved**
  - Since 2004
  - Over 90,000 grafts in eyes
  - Over 300 published reports
- **Dehydrated**
  - Since 2007
  - Over 70,000 grafts in eyes
  - Over 250,000 grafts in all





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Alternatives to Membranes

- **Bandage contact lens**, lubricants and antimicrobials for simple defects
- **Cenegermin**: FDA-approved for neurotrophic keratitis
- **Topical insulin** (off-label): healed 18 of 18 persistent defects vs 4 of 9 with membrane-extract drops
  - 2025 retrospective study, 27 eyes
- **Membrane-extract drops** (not amniotic fluid): no controlled trials
- **Tarsorrhaphy or sutured membrane** when inflammatory disease or no response

Buzzi et al., Clin Ophthalmol 2025; Sell et al., Am J Ophthalmol 2023

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Amniotic Membrane

What is it and how is it obtained

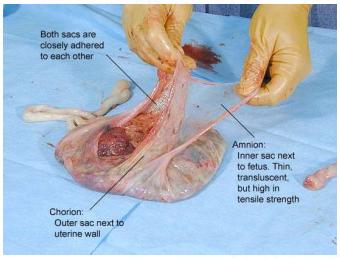
History of Use in Wound Care

- **1940**: fetal membrane used to repair conjunctival defects
- **1946**: amniotic membrane grafts for caustic burns
- **Early 1990s**: modern revival for ocular surface reconstruction
- **1997**: FDA recognition of AmnioGraft
- **2003**: FDA clearance of Prokera
- **Today**: cryopreserved and dehydrated forms placed in the office

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What is Human Amniotic Membrane?

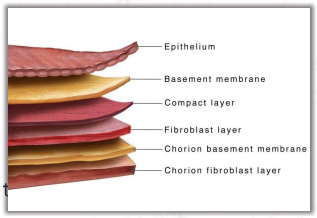
- A unique, avascular membrane separating the mother from fetus
  - **inner lining of placenta**
- Provides an incubating environment
  - **promoting cellular differentiation**
- Provides an immunological barrier
  - **prevents "foreign body" rejection**
- Mimics the conjunctiva



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Unique Grafting Characteristics

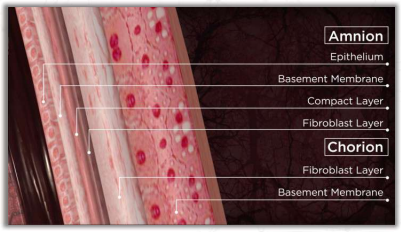
- Facilitates **epithelial cell migration**,
- Reinforces **adhesion of basal cells**,
- Promotes **epithelial differentiation**
- **Prevents epithelial apoptosis**.
- Can act as a **bandage contact lens**
  - **Reduces pain**
- In ocular use since the 1940s; revived in t
  - anti-inflammatory,
  - anti-fibrotic,
  - anti-vascularization
  - anti-scarring effects



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Amniotic Membrane - Profile

- Contains:
  - Structural proteins
  - Specialized proteins
  - **Cytokines**
  - **Growth Factors**



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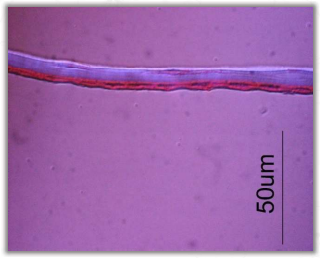
Structural Proteins

- AKA Extracellular Matrix
  - a structured substance produced by cellular activity
  - lies within the tissue, outside the cell
- **Collagens** Types I, III, IV, V, VII
- **Specialized proteins**
  - Elastin,
  - Fibronectin,
  - Laminin
  - proteoglycans, and
  - glycosaminoglycans



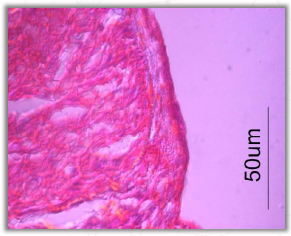
Specialized Proteins / Cytokines

- Cytokines
  - large category including chemicals & proteins
  - Aid in **maintaining corneal clarity**
- Interleukin 4, 10
  - Responsible for **inflammatory response and control**
- Tissue Inhibitors to Metalloproteinases (TIMPS) 1,2,4
  - **Suppress MMP**



Growth Factors

- A subset of cytokines
  - responsible for eliciting a cell response and cell-to-cell communication
- Includes
  - **Fibroblast Growth Factor** (FGF)
  - **Transforming Growth Factor Beta** (TGF-β)
  - **Epidermal Growth Factor** (EGF)
  - **Platelet-derived Growth Factor** (PDGF A&B)
- **Promotes and accelerates epithelialization**



How it works – Key Points

- Cytokines
  - Cell **signaling molecules** that aid cell to cell communication in immune responses and
  - **stimulate the movement of cells towards sites of inflammation**, infection and trauma
- Growth Factors
  - Proteins that bind to receptors on the cell surface, with the primary result of
  - **activating cellular proliferation and/or differentiation**



Cryopreserved Screening

Blood

- ✓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)

Donor

- ✓Infectious,
- ✓Malignant,
- ✓Neurological
- ✓Auto-immune
- ✓and other exposures or social habits

Processing

- Aseptically processed according to current:
  - **Good Tissue Practices** (cGTP)
  - **Good Manufacturing Practices** (cGMP)
- **Cryopreserved**
  - Stored in validated medium of **Dulbecco's Modified Eagle Medium**/Glycerol (1:1)
  - Containing Ciprofloxacin and Amphotericin B.
  - Prokera: FDA-cleared Class II device
  - 1 year shelf life in freezer



Dehydrated Screening

Blood

- ✓HIV-1 & HIV-2 Antibody
- ✓HIV-1 (RNA-NAT)
- ✓Hepatitis B Surface Antigen (HBsAg)
- ✓Hepatitis B Core Antibody (HBcAb)
- ✓CMV Total Antibody
- ✓Hepatitis C Antibody (HCVAb)
- ✓Hepatitis C Virus (HCV, RNA-NAT)
- ✓Syphilis (RPR)
- ✓HTLV I & II Antibody (HTLV I/II Ab)

Donor

- ✓Screened by Surgical Biologics medical director
- ✓Pathologist certified by the American Board of Pathology in
  - ✓clinical pathology
  - ✓blood banking/transfusion medicine

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Dehydrated Processing

- **Serological testing**
  - ➢per FDA and AATB
- Placenta is **recovered in OR** environment
  - ➢Immediately following child delivery
  - ➢Placed sterile container w/ hypertonic solution
- **Transferred** to Class 100 bio safety cabinet
  - ➢Gentle washes and sterile water rinses to remove unwanted biological material
- Tissue **stabilization**
  - ➢accomplished by dehydration
- Packaged in **inner & outer peel pouch** system
  - ➢then dosed with Electron-Beam irradiation
  - ➢terminal sterility > 5 year shelf life

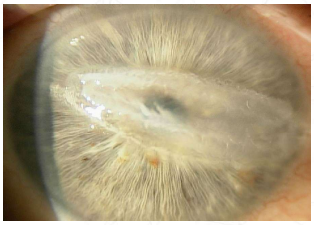


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Indications for usage

Indications: Diseases with Pre-existing Epithelial Defects

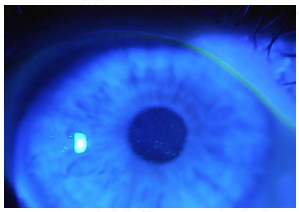
- To **promote wound healing and reduce complications** (debridement is optional)
- Neurotrophic Persistent **Corneal Epithelial** Defect
- Post-Infectious Recalcitrant **Corneal Ulcers** (e.g. herpetic, vernal, and bacterial)
- **Non-Healing Epithelial Defect** After PRK/PTK
- Acute **Chemical / Thermal Burns**
- Acute **Stevens-Johnson Syndrome**/Toxic Epidermal Necrolysis
- Corneal melt or impending perforation (co-manage)



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Indications: Diseases without Epithelial Defects

- To prevent further damage and promote regeneration (no debridement/PTK)
- **Dry Eye Syndrome**
- **Superficial (Punctate) Keratitis**
- **Filamentary Keratitis**
- Radiation Keratitis; whorl pattern indicative of limbal stem cell injury
- Exposure (Graves) Keratopathy



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Indications: Diseases w/ Unhealthy Epithelium or Basement Membrane

- To promote regeneration (after debridement / PTK)
- **Recurrent Corneal Erosion**
- Salzmann's Nodular Degeneration
- Bullous Keratopathy during/following DSEK
- Haze after PTK
- Partial Limbal Stem Cell Deficiency
- **Corneal Dystrophy** (e.g., Reis-Bücklers)



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When to use amniotic membranes?

- Virtually any **corneal or conjunctival** surface disease that involves **inflammation** may benefit from the use of an amniotic membrane
- The literature supports favorable outcomes in almost every aspect **of inflammatory or infectious keratitis**
- In most patients and most conditions, **early placement** of an amniotic membrane is generally more favorable to the healing of the ocular surface

Cryopreserved vs Dehydrated

- **220 persistent epithelial defects**: resolved after one application in **46.5% cryopreserved vs 44.1% dehydrated** (P = .727)
- Comparable resolution, improvement and need for surgery
- **Inflammatory disease** predicted non-resolution
- Cryopreserved keeps **HC-HA/PTX3**; newer dehydration methods preserve more matrix
- Small series (56 eyes): **more ring discomfort** with cryopreserved

Sell et al., Am J Ophthalmol 2023 (retrospective); single-practice comparison, Digital J Ophthalmol (retrospective)

Evidence: Corneal Ulcers

- Systematic review (2025): **9 studies, 322 eyes**
- Epithelial healing **82% to 93%** in most studies
- Refractory neurotrophic ulcers: **54%** healed
- **Multilayer** grafts healed faster than single layer
- **Pain relief** within 48 hours
- Evidence quality **limited**: small, varied studies

Systematic review of AMT in corneal ulcer healing, 2025 (PMC12270348)

Evidence: Timing Matters

- **Chemical burns**: dehydrated membrane within 48 hours healed **23 of 23 eyes** in one month, including grade IV
- **Severe SJS**: membrane at 7 to 14 days **prevented limbal stem cell deficiency** (randomized trial)
- Supports **early placement**
- In-office, sutureless placement makes early treatment practical

Lotfy et al. and Sharma et al., as reviewed in a 2025 narrative review (PMC12167220)

Treatment Guidelines

- **Complete success** of an amniotic membrane placement procedure is defined as complete healing of the ocular surface after one application of the allograft without further intervention
- **Partial success** is partial healing of the ocular surface requiring further intervention
  - Bandage contact lens treatment
  - Repeat amniotic membrane placement
  - Topical medical therapy
- **Failure** is defined as lack of documented improvement with amniotic membrane therapy or discontinuation of the therapy session prior to demonstrable improvement

Treatment Protocol

- Perform the placement procedure early in the day if possible
- **Telephone follow-up** or in-office examination 4-6 hours later
  - No hyper-lacrimation
  - No foreign body sensation
  - No conjunctival hyperemia
  - No ocular pain
- **1-day postoperative** examination the next day
- **Daily postoperative examinations** until the amniotic membrane is absorbed and cannot be visualized
- If the allograft is still present after four days, terminate the therapy session

Placement

Insertion and Removal

Cryopreserved Insertion Technique


1. Apply anesthetic


2. Hold upper eyelid


3. Have patient look down


4. Insert into superior fornix

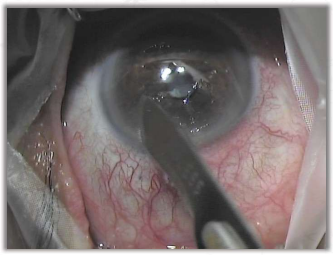

5. Pull lower lid down and slide under


6. Check centration with microscope

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Step 1: Prep and Denude

- Patient in supine position
- **Place the lid speculum**
- Apply topical anesthesia
- **Denude** 1-2 mm of epithelium surrounding defect with gentle blade or Weck-Cel sponge



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Step 2: Placement of Dehydrated

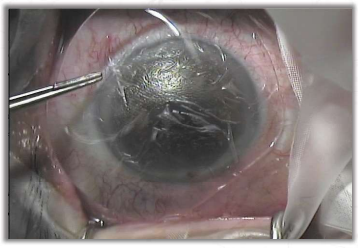
- Maintain **dry ocular surface**
- Center graft on cornea
- Place **dull side down**
- Gently smooth using traction, counter traction
- 1-2 mm over peripheral conj
- **Disregard small creases and bubbles**



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Step 3: Placement of Lens

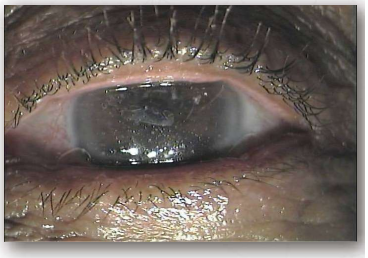
- 18, 16 or 14mm BCL
- Non tooth forceps
- **Center lens over Dehydrated**
- Maintain centration of disk over cornea



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Step 4: Finish

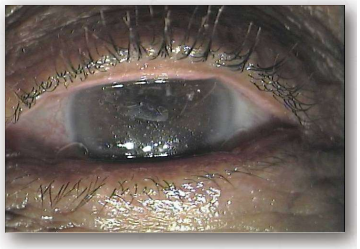
- Gently remove speculum
- **Request several blinks**
- Disregard small bubbles, creases
- **Apply appropriate meds**
- < 10-minute procedure



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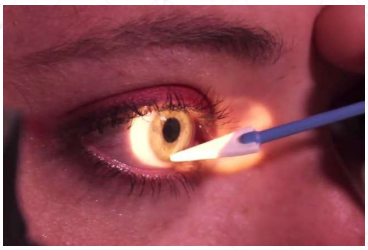
Can do without Speculum too

- Have staff hold lid open
- No chances of scratching eye with speculum



Alternate Step 1: Prep and Denude

- Patient seated
- Apply topical anesthesia
- **Denude** 1-2 mm of epithelium surrounding defect with **Weck-Cel sponge**



Alternate Step 2: Placement of Dehydrated

- Dry back surface of CL
- Center graft on CL
- Place **dull side up**
- Gently smooth
- **Disregard small creases and bubbles**



Alternate Step 3: Placement of Lens

- 18, 16 or 14mm BCL
- Insert CL w/ Dehydrated
- **Maintain centration** over cornea



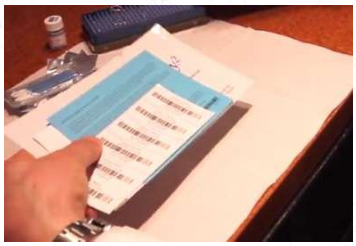
Alternate Step 4: Finish

- Request several blinks
- Disregard small bubbles, creases
- Apply appropriate meds
- < 10-minute procedure



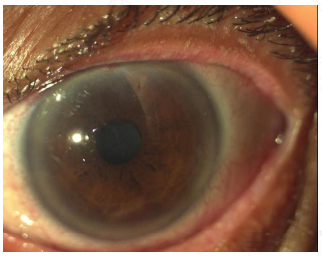
Additional steps

- Fill out paperwork



Dehydrated: Management

- Follow up: 48 hours
- Dehydrated dissolves during healing
- Absorption: 7-14 days
- Rx: Doctor discretion, judgment

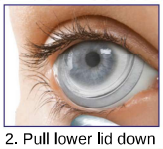


Dehydrated: Removal and Medications

- **Remove the bandage lens** once the membrane has dissolved, or at your discretion
- Confirm **epithelial closure** and clarity at removal
- If membrane remains, **rinse** and re-evaluate
- **Continue disease-specific therapy** (antimicrobial, anti-inflammatory) as indicated
- **Antibiotic prophylaxis** while epithelium is open
- **Document** removal date and membrane status

Cryopreserved Removal Technique


1. Apply anesthetic


2. Pull lower lid down


3. Lift lower edge


4. Ask patient to look down


5. Apply gentle pressure on upper lid


6. Slide out

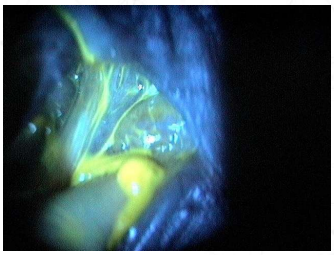
Use in Dry Eye

Use in Dry Eye Syndrome

- Dry eye syndrome evolves through a sequence of four milestones:
  - **Loss of water from the tear film** w/ increase in osmolarity
    - Increased **conjunctival epithelial desquamation**
      - Increased **corneal epithelial desquamation**
        - **Destabilization** of the cornea-tear interface

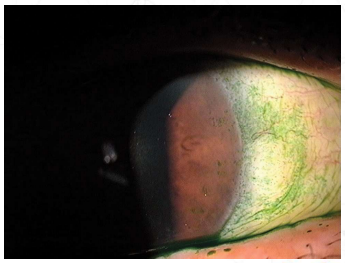
Loss of Water from the Tear Film

- Loss of water from the precorneal tear film results in **decreased tear film volume** and is associated with debris in the tear film
- **Dehydrated mucus** that has precipitated in the inferior fornix indicates severe loss of water from the tear film



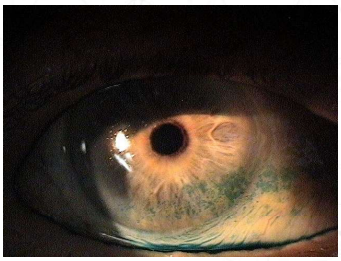
Conjunctival Epithelial Desquamation

- Abnormal increase in **conjunctival epithelial sloughing** results in immature conjunctival epithelial cells moving onto the surface of the eye
- As the desquamation accelerates, the **damaged cells release inflammatory mediators** onto the surface of the eye and the inflammatory process begins



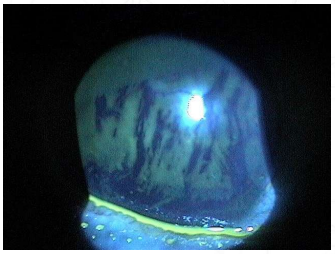
Corneal Epithelial Desquamation

- Continued exposure to the osmotic gradient produced by **high tear film osmolarity** will eventually damage the cornea
- As corneal desquamation accelerates, the damaged cells perpetuate the inflammatory process by **releasing inflammatory mediators** onto the ocular surface



Destabilization of Cornea-Tear Interface

- Abnormal tear film break-up time indicates tear film instability secondary to **loss of epithelial microvilli**
- The corneal epithelial changes required to cause tear film instability occur late in the natural history of dry eye syndrome



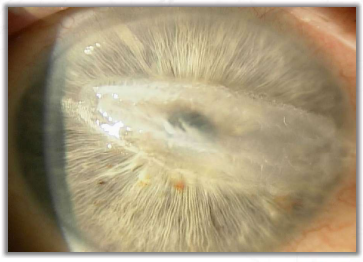
Many Other Uses

Case studies from my own patients...

Clinical Case: Thermal Burn

Presentation

- 68 YO WM
- Hit in eye with hot welding rod
- Severe lineal thermal burn over central corneal



Clinical Case: Thermal Burn

24 hours later

- Membrane in place
- Significant healing
- Patient pain free



Clinical Case: Thermal Burn

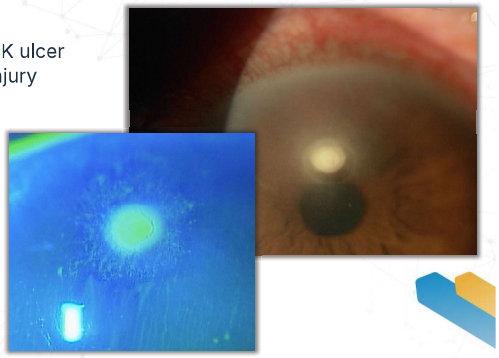
5 day follow up
- Membrane removed
- Wound completely resolved
- Minimal haze and scarring
- 20/25 uncorrected



Clinical Case: Corneal Ulcer

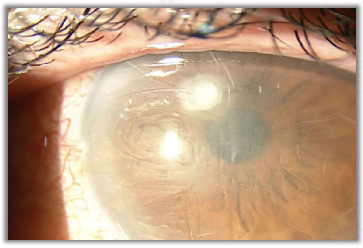
Presentation
- 54 YO HM w/ Severe K ulcer
- infection after work injury

- Hypopyon
- Stromal haze
- Large defect
- Heavy staining



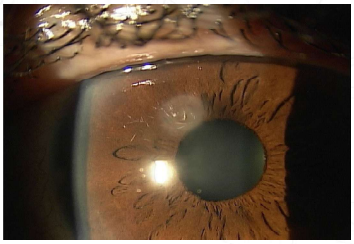
Clinical Case: Corneal Ulcer

2 day follow up
- Membrane in place
- Haze clearing
- Vision normalizing



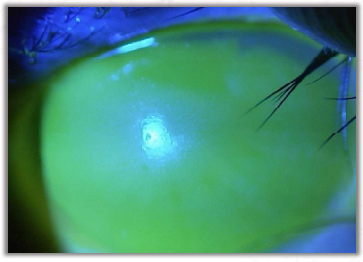
Clinical Case: Corneal Ulcer

20 day follow up
- Membrane removed day 5
- Haze cleared
- Vision normal



Clinical Case: Alkali Burn

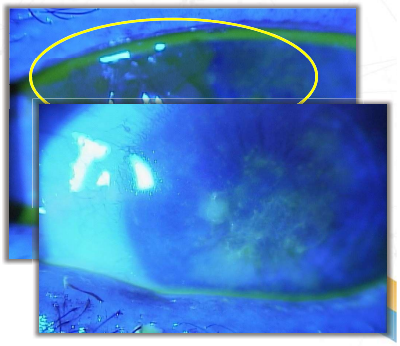
Presentation
- 48 YO HM
- Using a pressure washer to clean a building
- Severe alkali burn
- Affecting 99% of cornea



Clinical Case: Alkali Burn

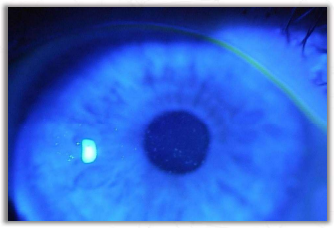
11 day follow up
- Almost re-epithelialized
- Small piece of membrane visible upon removal of bandage lens

Rinsed well
- Mild edema and swelling
- Minimal pain
- Near normal vision



Clinical Case: Alkali Burn

28 day follow up
- Nearly resolved
- Minimal SPK
- 20/30 uncorrected acuity



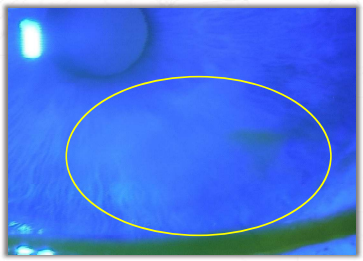
Clinical Case: HSVK

Presentation
- 65 YO WF
- Herpes simplex keratitis
- Recurrent, non healing
- Vascularization inf/temp



Clinical Case: HSVK

7 day follow up
- Membrane dissolved
- Epithelial defect gone
- Vascularization mostly gone

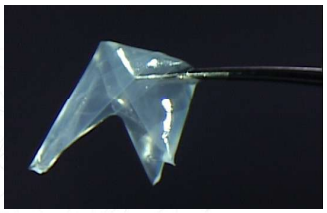


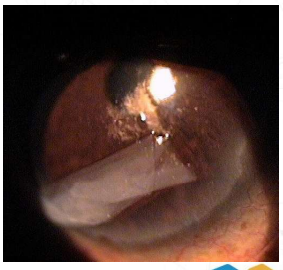
Potential Complications

- **Patient intolerance**
  - Cryopreserved allograft (10% - 50%)
- **Poor surgical technique**
  - Allograft instability
  - Dislodged allograft
  - Superficial corneal lacerations
- **Poor cornea-contact lens relationship**
  - Red eye secondary to overnight contact lens wear
- **Rejection of transplant tissue**
  - A type II allergic reaction
  - Cytotoxic hypersensitivity

Dislodged Allograft

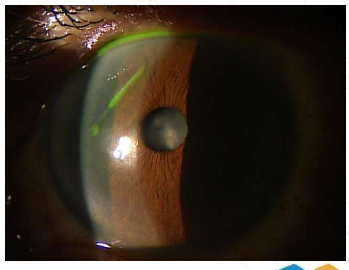
- Clinical appearance at follow-up
- Chronic **foreign body sensation**
- **Mild ocular discomfort**
- Treatment is to **discontinue** the amniotic membrane therapy





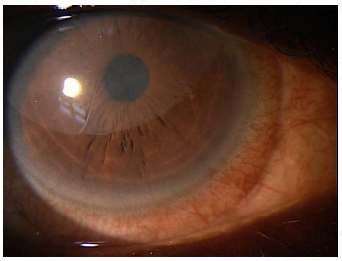
Superficial Corneal Laceration

- **Superficial corneal injury** associated with a less than ideal (i.e., wrinkled) dehydrated amniotic membrane allograft placement
- Onset of **moderate ocular discomfort** is **4-6 hours after** placement procedure
- Best treatment option is to **discontinue** dehydrated amniotic membrane therapy



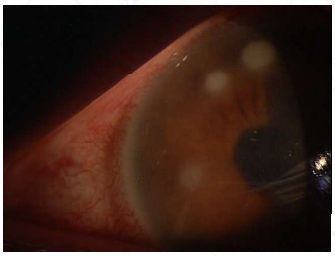
Poor Cornea-Contact Lens Relationship

- Cornea-contact lens relationship results in a **"tight" lens fit** peripherally
- **Base curve that is too steep** allows for allograft migration superiorly
- Treatment options
  - discontinue AM therapy
  - **Try again with different CL**



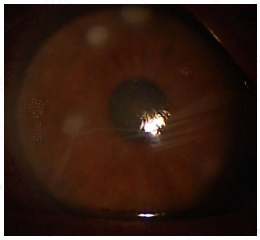
Rejection of Transplant Tissue

- Moderately-severe to severe **pain**
- Conjunctival **hyperemia**
- Loss of corneal stromal transparency **decreases vision**
- **Eyelid edema**
- Multiple, **greyish-white large mid-peripheral corneal infiltrates**
- **Elevated IOP**
- Onset **2-12 hours after placement** procedure



Cytotoxic Hypersensitivity

- A **type II allergic reaction** that involves the interaction of immunoglobulins with foreign or autoantigens closely associated with cell membranes
- In this condition, **the antigen is the amniotic membrane allograft**
- **Allograft is recognized as foreign** and IgG or IgM antibodies are formed which react with and activate the serum complement enzymatic cascade
- **Corneal stromal cell lysis may result** from complement activation and from recruitment of leukocytes



Coding & Billing

Coding and Billing: CPT

- **65778**: placement of amniotic membrane on the ocular surface for wound healing; **self-retaining**
- **65779**: same; **single layer, sutured**
- **65780**: ocular surface reconstruction; amniotic membrane transplantation, **multiple layers**
- Report **laterality** (RT / LT)
- Allowable varies: look up the code in the **CMS Physician Fee Schedule** for your locality

Billing: What Not to Bill

- Membrane **product cost is bundled** into the CPT payment
- **V2790** on a Medicare claim results in a denial
- **Amniotic drops** are not a membrane: never bill them as one
- **Skin-substitute Q-codes** and their 2026 payment change do not apply to ocular CPT codes
- **Pterygium**: report 65426; do not add 65778 or 65779 for the membrane
- **65780** is for reconstruction (limbal stem cell deficiency, extensive burns, SJS), not routine dry eye or ulcers

Third-party coding guide, 2026; confirm with your Medicare contractor

Common ICD-10 Diagnoses

- **H16.23-** Neurotrophic keratoconjunctivitis
- **H16.0-** Corneal ulcer (H16.00- unspecified)
- **H18.83-** Recurrent erosion of cornea
- **H04.12-** Dry eye syndrome
- **T26.6-** Corrosion of cornea and conjunctival sac (chemical burn)
- **L51.1** Stevens-Johnson syndrome

Checked against FY2027 ICD-10-CM. Add laterality; T26 codes also need a 7th character (A, D or S).

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Documentation

- **Diagnosis**, laterality, size and location of defect
- **Failed conservative therapy** and how long it was tried
- **Medical necessity**: why a membrane, not a bandage lens alone
- **Product**: type, size, lot or tracking number
- **Procedure note** and **follow-up plan**, including membrane status at removal

Payer example: defect not responding in 2 days; severe dry eye (DEWS 3 to 4) after steps 1 to 3; moderate or severe chemical burn

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Summary

- Two forms: **cryopreserved** (ring) and **dehydrated** (with bandage lens)
- **Comparable** outcomes for persistent epithelial defects
- **Early placement** helps; inflammatory disease predicts failure
- Know the **complications** and when to stop therapy
- **Document** necessity and report the right CPT code
- Amniotic fluid drops are **not FDA approved** and **not a membrane**

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Questions?

- **peter@pppnow.com**

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