Bridging Regeneration and Repair: The Role of Amniotic Membrane in Corneal Healing

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Omni Eye Specialists

Part of the ICON Network

Financial Disclosures

- Speaker for Dompé (does not make amniotic membranes)

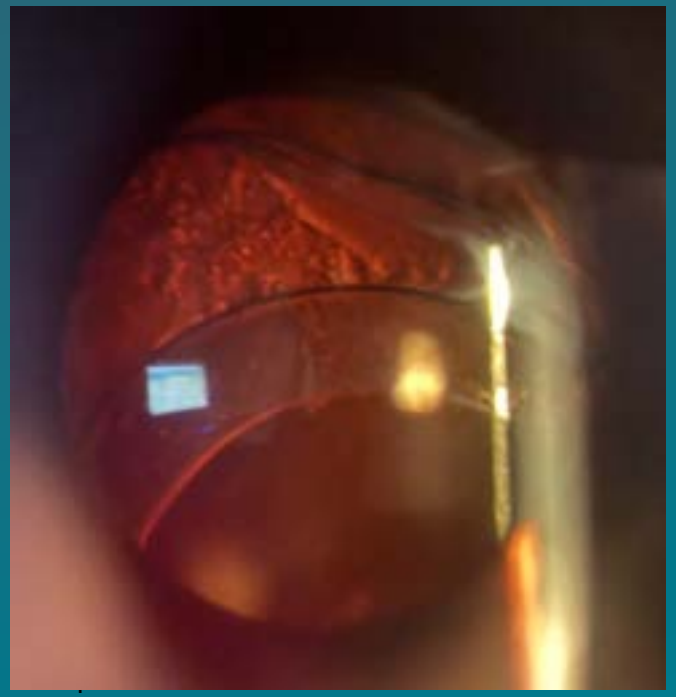
About Me

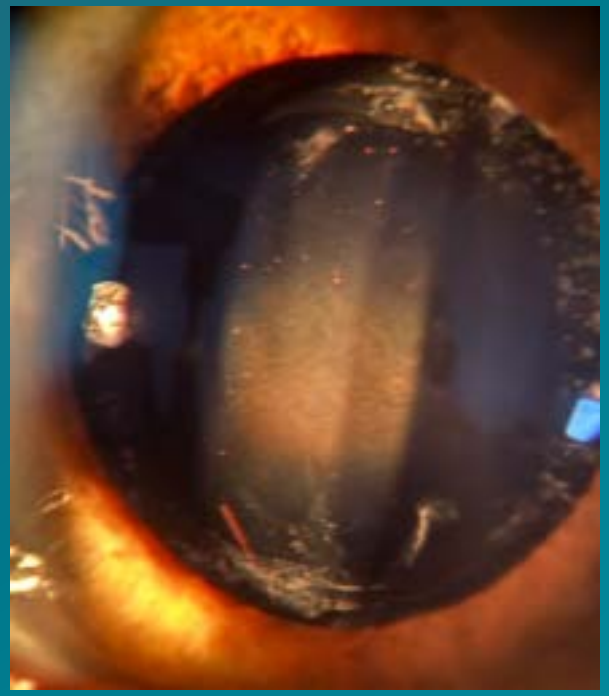
- Duke for undergraduate, medical school, residency, and cornea fellowship
- Biggest Duke Basketball fan in the state of Colorado

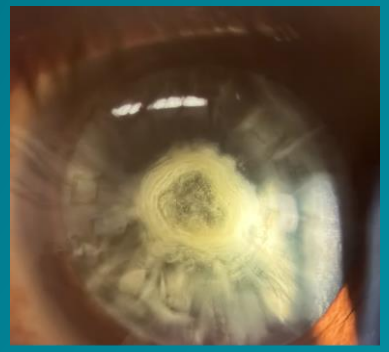


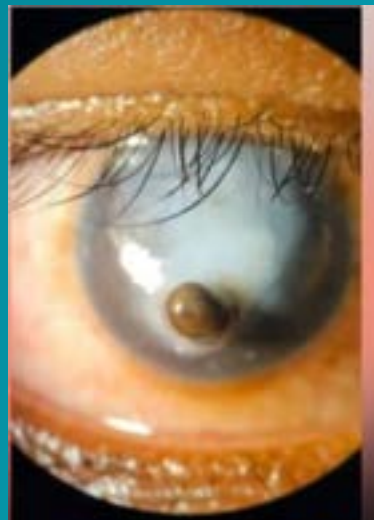

Surgeries I Offer

- Complex cornea, cataract, and iris
- Refractive cataract surgery, LASIK/ICL/CLE
- YouTube channel: youtube.com/@jamestianmd









Amniotic Membrane Tissue

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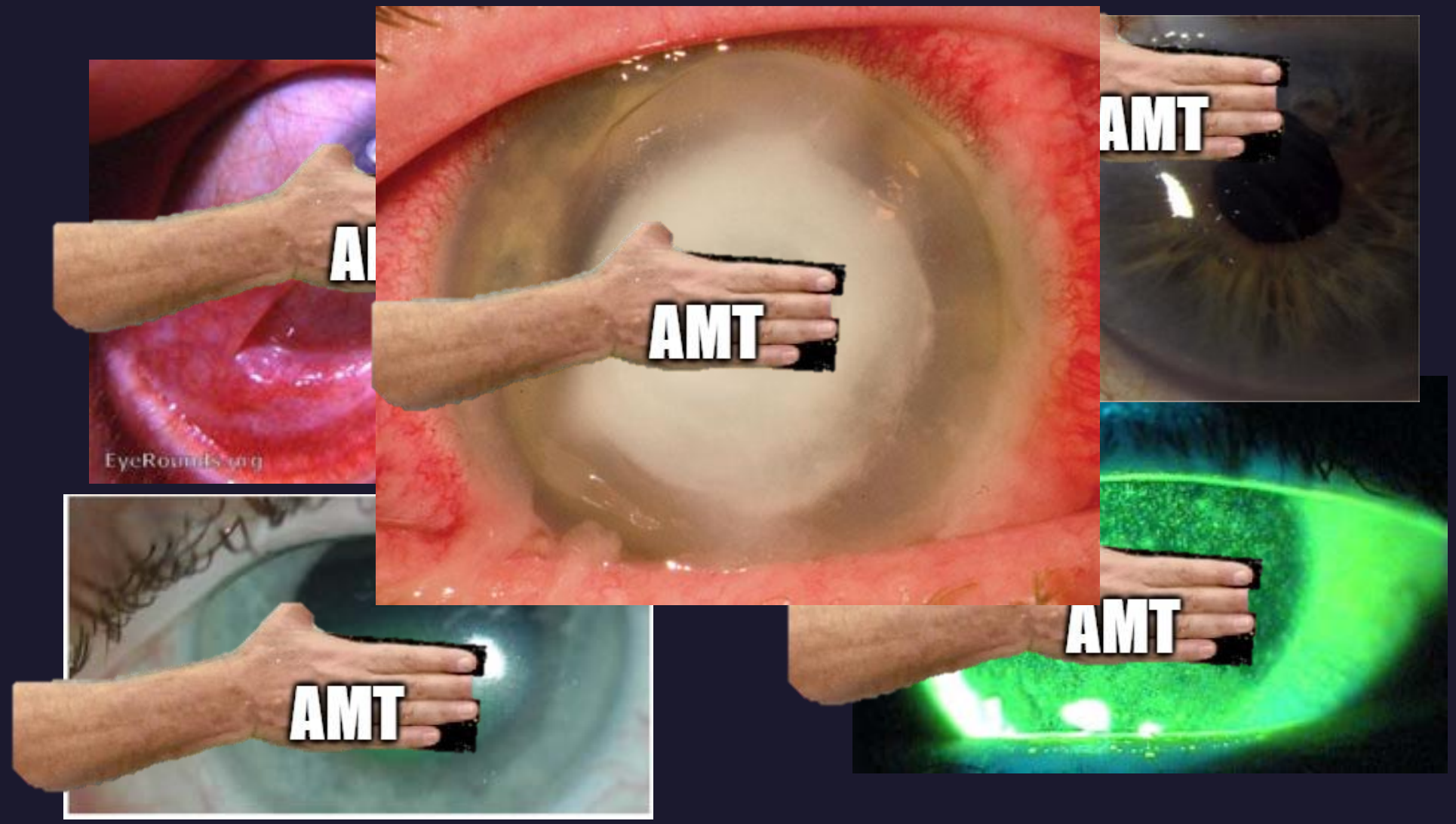
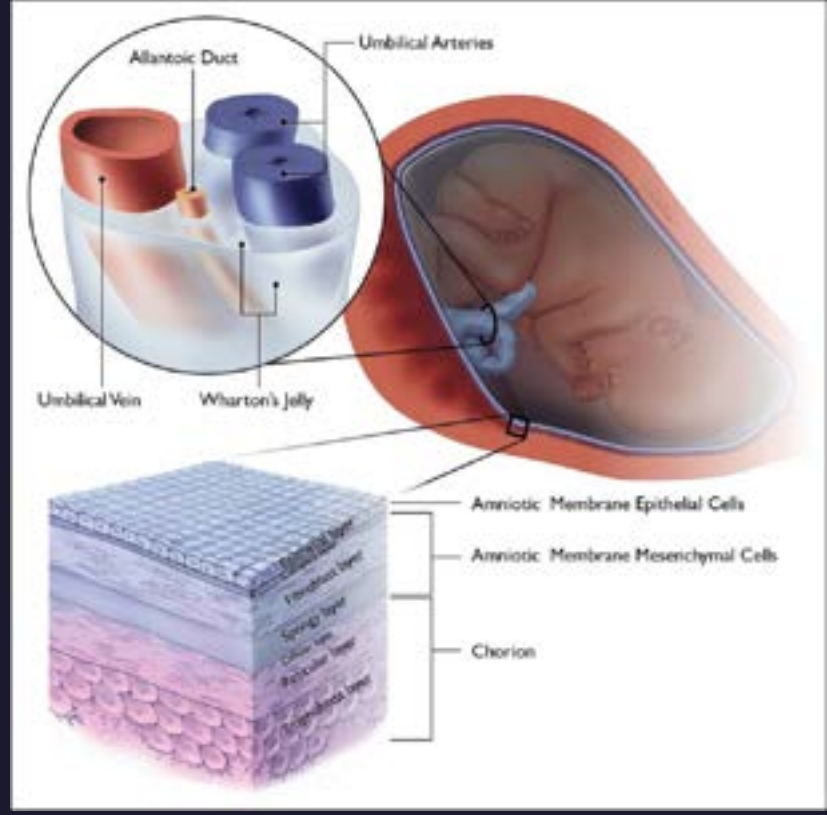


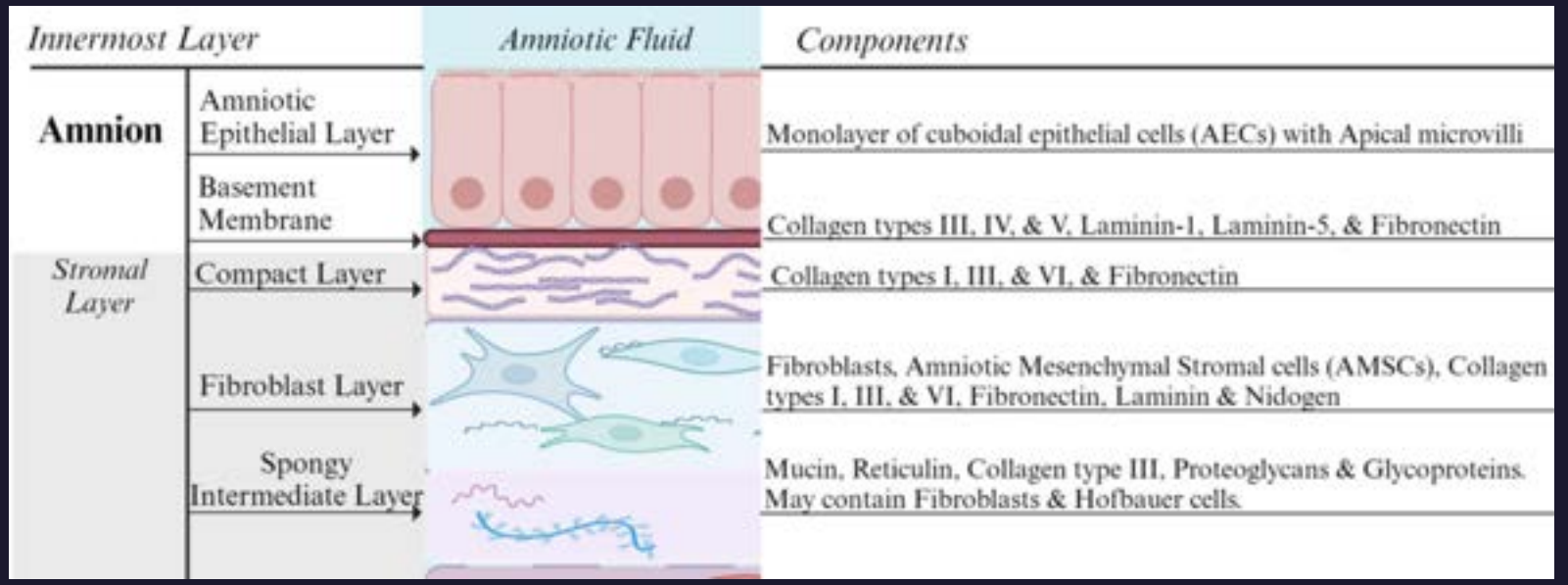
What is Amniotic Membrane?

- **Amniotic membrane** tissue is the innermost layer of the **placenta**

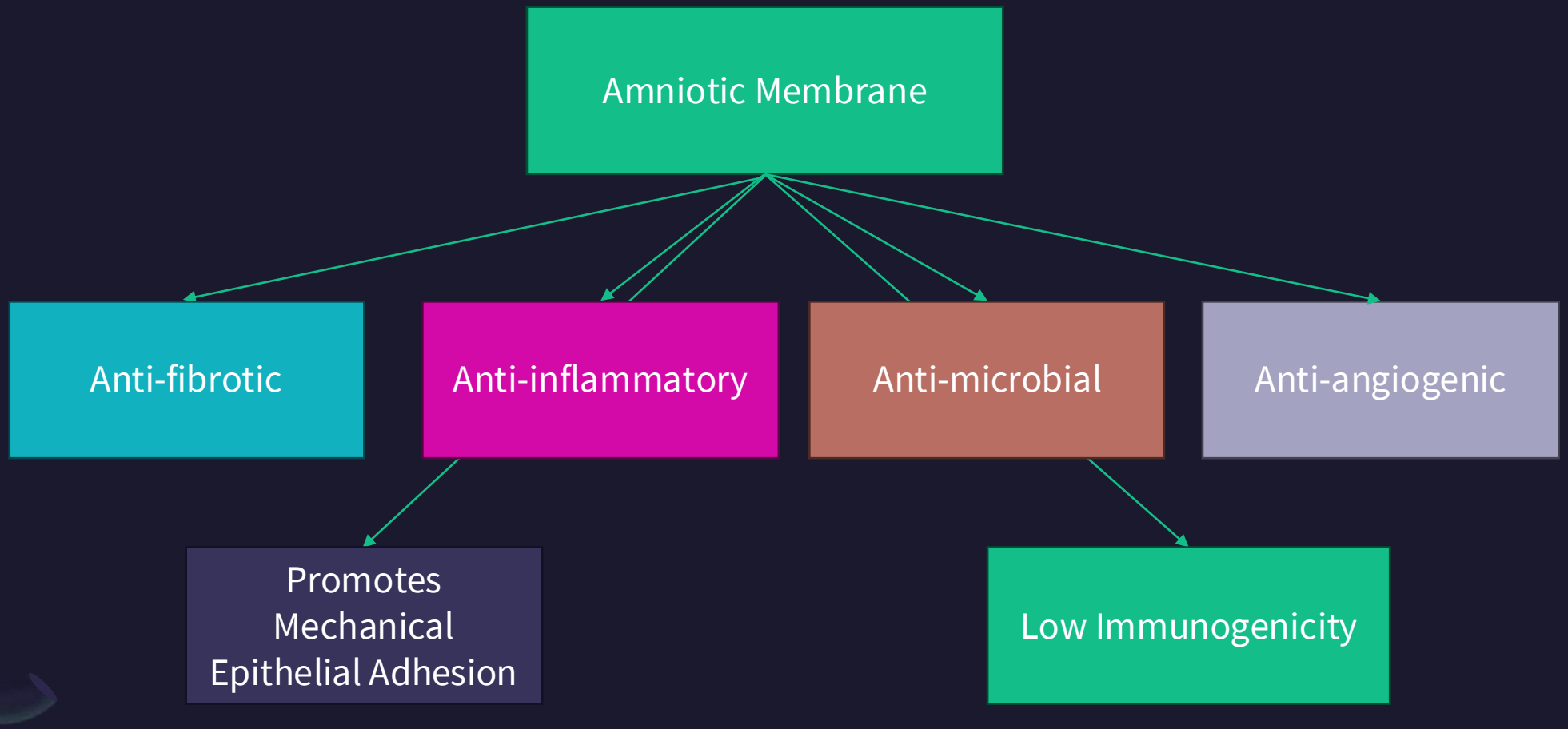
Three layers

- Epithelium
- Basement membrane
- Stroma



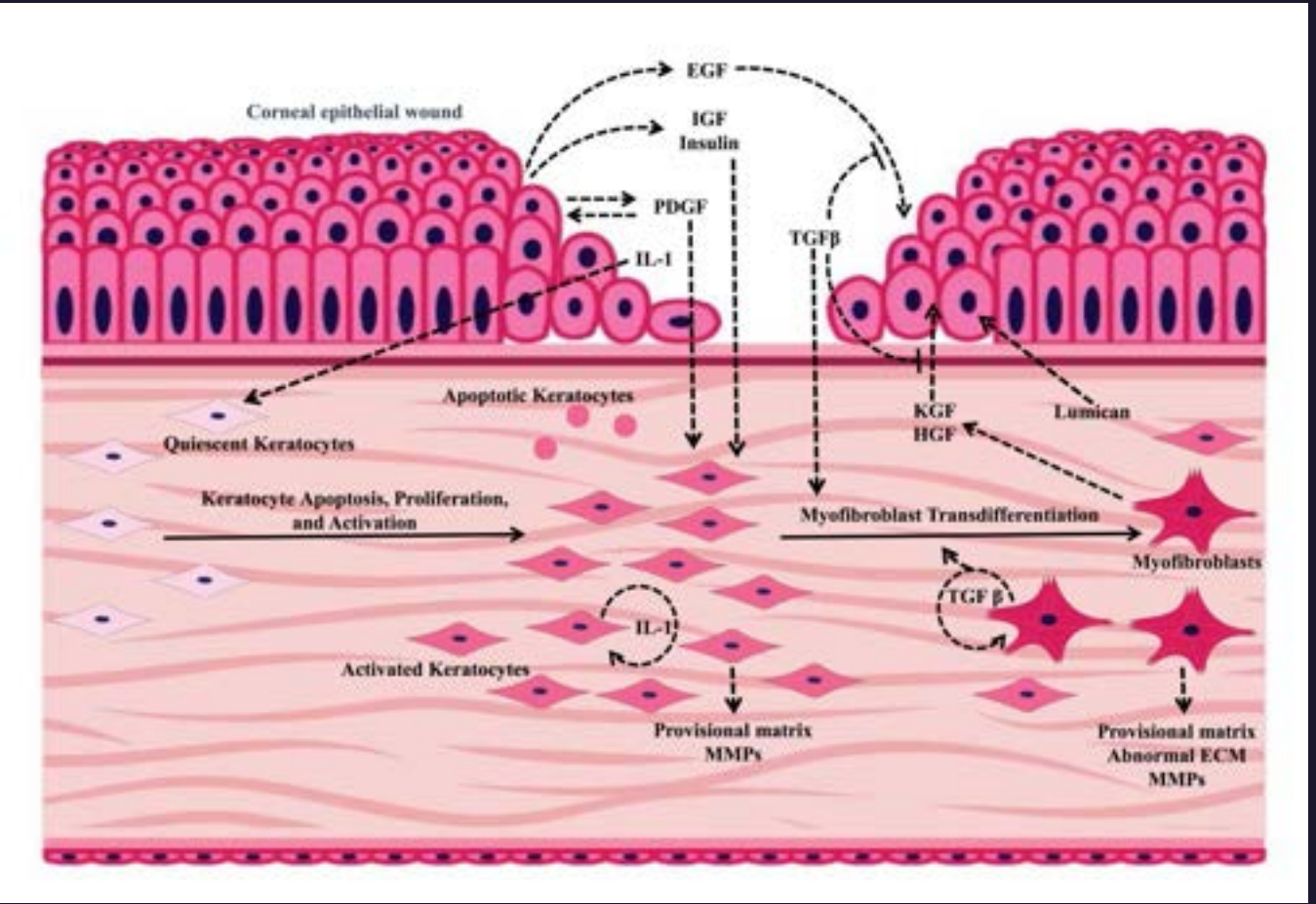


How does it work?



Anti-Fibrotic & Anti-Inflammatory

- **Anti-Fibrotic**
  - Suppresses **TGF-b** signaling and inhibits expression of various TGF-b isoforms
    - Inhibiting **fibroblast differentiation into myofibroblasts**
- **Anti-inflammatory**
  - Inhibits IL-1a, IL-2, IL-8, IL-10, IFN-y, TNF, and PDGF
  - Inflammatory cells may get trapped in AM and undergo apoptosis as well

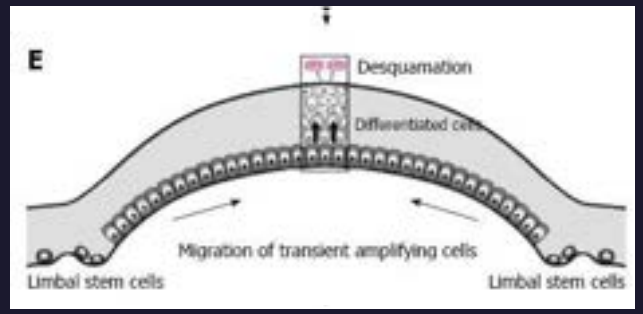


Anti-Microbial and Anti-Angiogenic

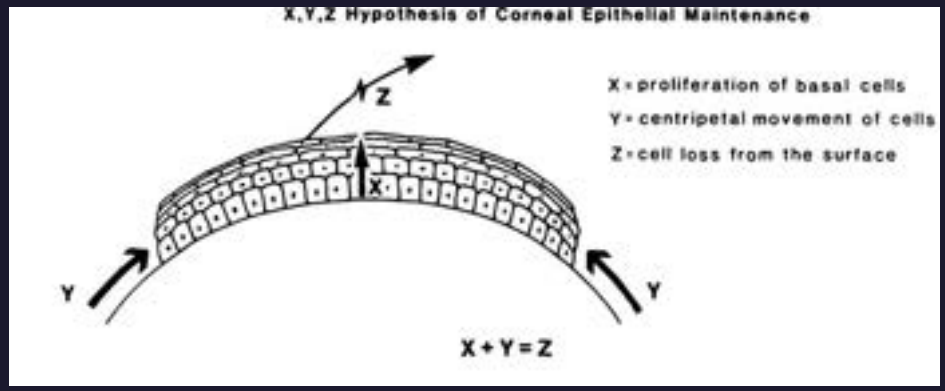
- **Anti-microbial** → provides both a **physical barrier** to infection but also contains anti-microbial peptides and defensins
- **Anti-angiogenic** → contains potent anti-angiogenic compounds, IL-10, metalloproteinase inhibitors, which **limit neovascularization**

Mechanical Properties & Epithelialization

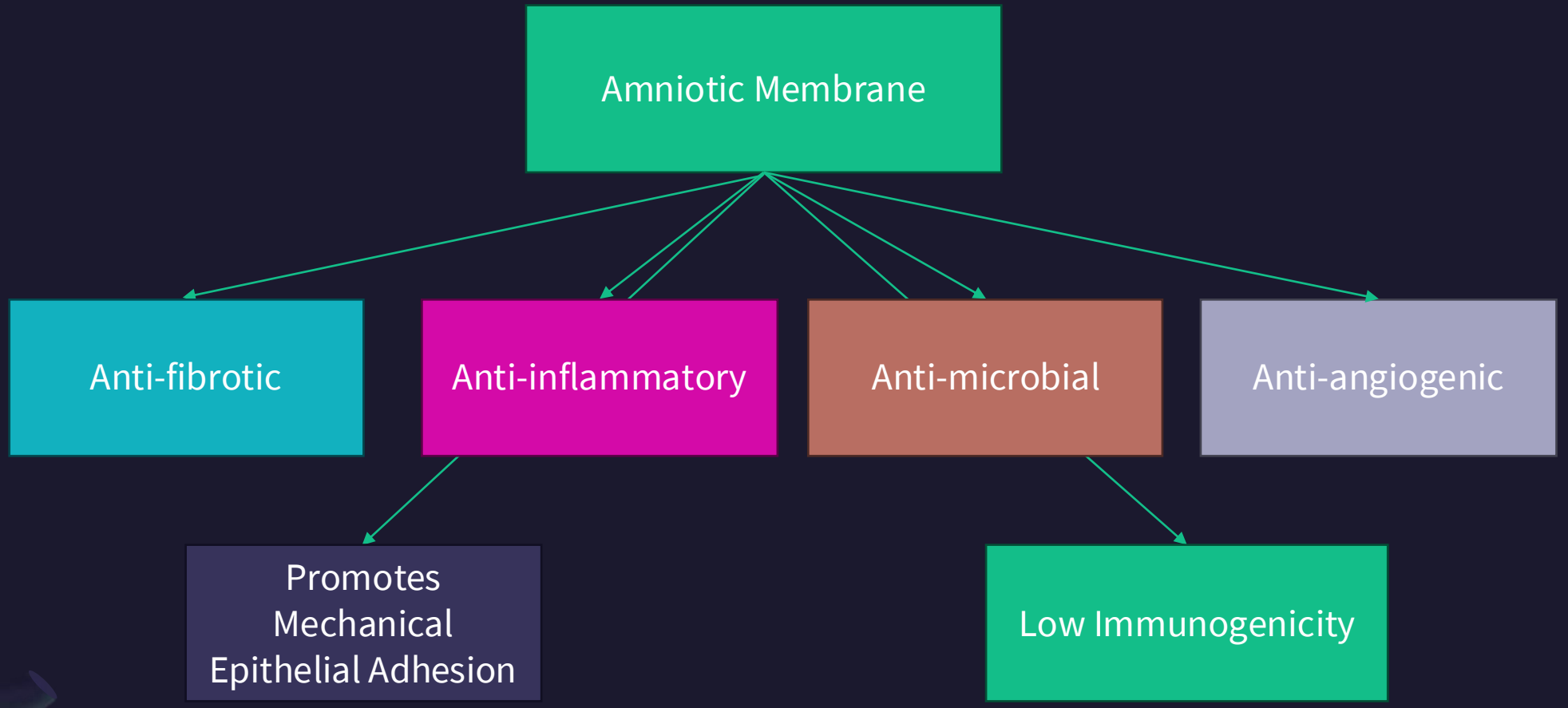
- The AM basement membrane is very similar to the conjunctival and corneal basement membrane
  - Similar collagen make-up
- Provides **scaffolding and substrate** for epithelial cells to grow over
- Promotes **adhesion** of basal epithelial cells



- AMT promotes **epithelization** through EGF, HGF, and KGF
- **Prevents** epithelial cell **apoptosis**



How does it work?



Low Immunogenicity→ has limited expression of HLA, **no need for immune suppression**

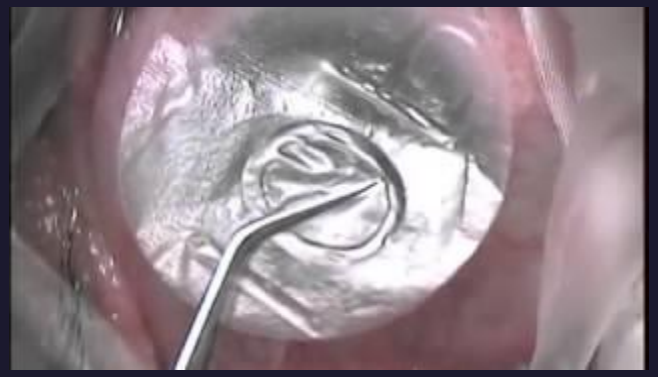
Cryopreserved

- Stored in **glycerol** solution and frozen
- Typically refrigerated, but recent products can be stored at room temperature due to gamma-irradiation
- Preserves **growth factors** better than other methods.
- Better preserved basement membrane

Cooke M, Tan EK, Mandrycky C, He H, O'Connell J, Tseng SC. Comparison of cryopreserved amniotic membrane and umbilical cord tissue with dehydrated amniotic membrane/chorion tissue. J Wound Care. 2014 Oct;23(10):465-74, 476.

Dehydrated

- Amniotic membrane is flash frozen to 50-80 C then dried under high vacuum
- Results in **thinner, longer shelf-stable** tissue
- Has **less growth factors** than cryopreserved



Clinical Indications

- Neurotrophic Keratopathy
- Chemical/Thermal Burns
- Persistent Epithelial Defects
- Severe Dry Eye (especially inflammatory)
- Surgical Indications

Clinical Indications

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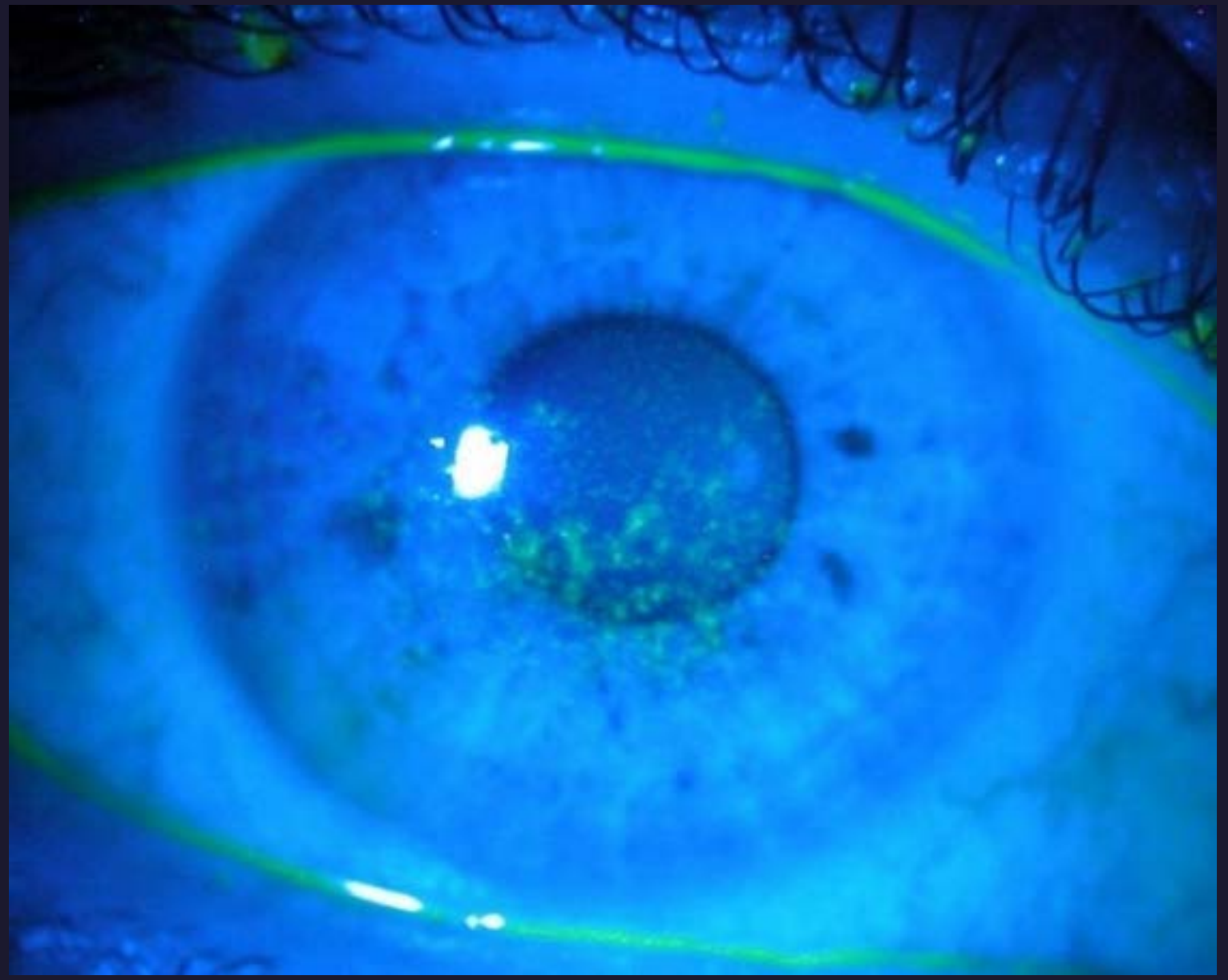
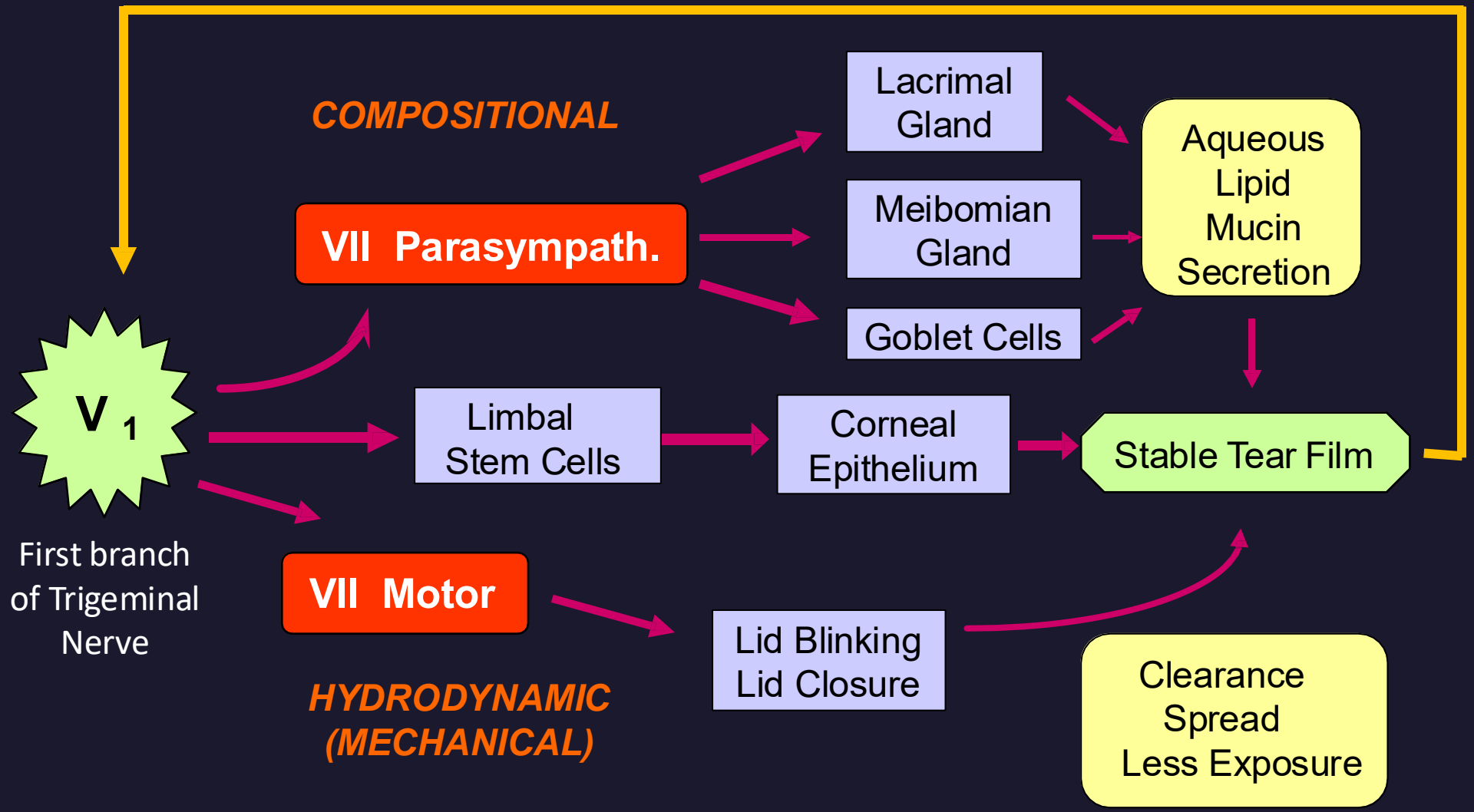
Stain Without Pain

- As opposed to pain without stain
- Or stain AND pain

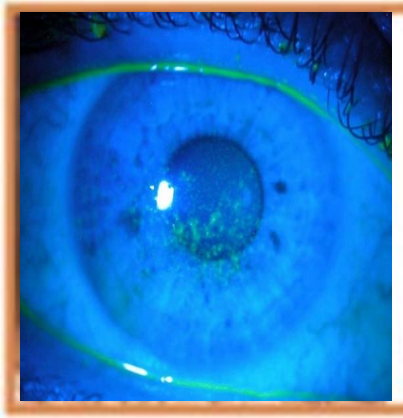


Aqueous Tear Deficient DED Leads to NK



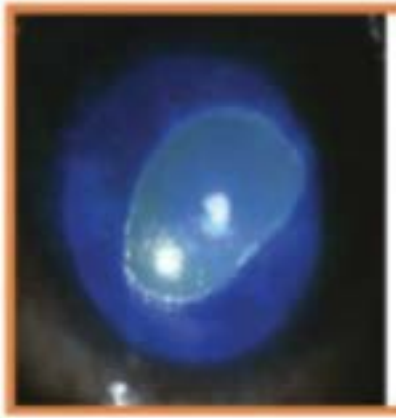
Tseng, S., and Tsubota, K. Important concepts for treating ocular surface and tear disorders. *Am J Ophthalmol.* 1997; Dec 124(6):825-835.

Mackie Classification



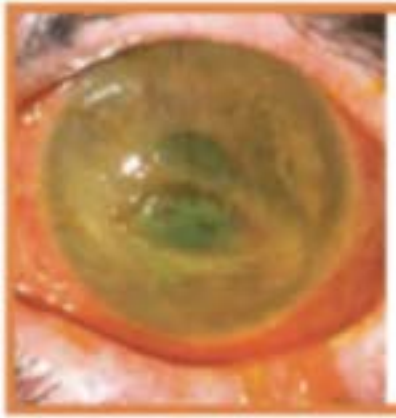
STAGE 1 (Mild)

Punctate keratitis



STAGE 2 (Moderate)

Persistent epithelial defect (PED)

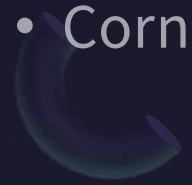


STAGE 3 (Severe)

Corneal ulcer

Neurotrophic Keratitis Treatment

- Artificial tears, punctal occlusion, serum tears
- Cenergemin (recombinant human nerve growth factor)
- Amniotic membrane
- Tarsorrhaphy
- Address structural eyelid issues
- Scleral lenses
- Corneal neurotization

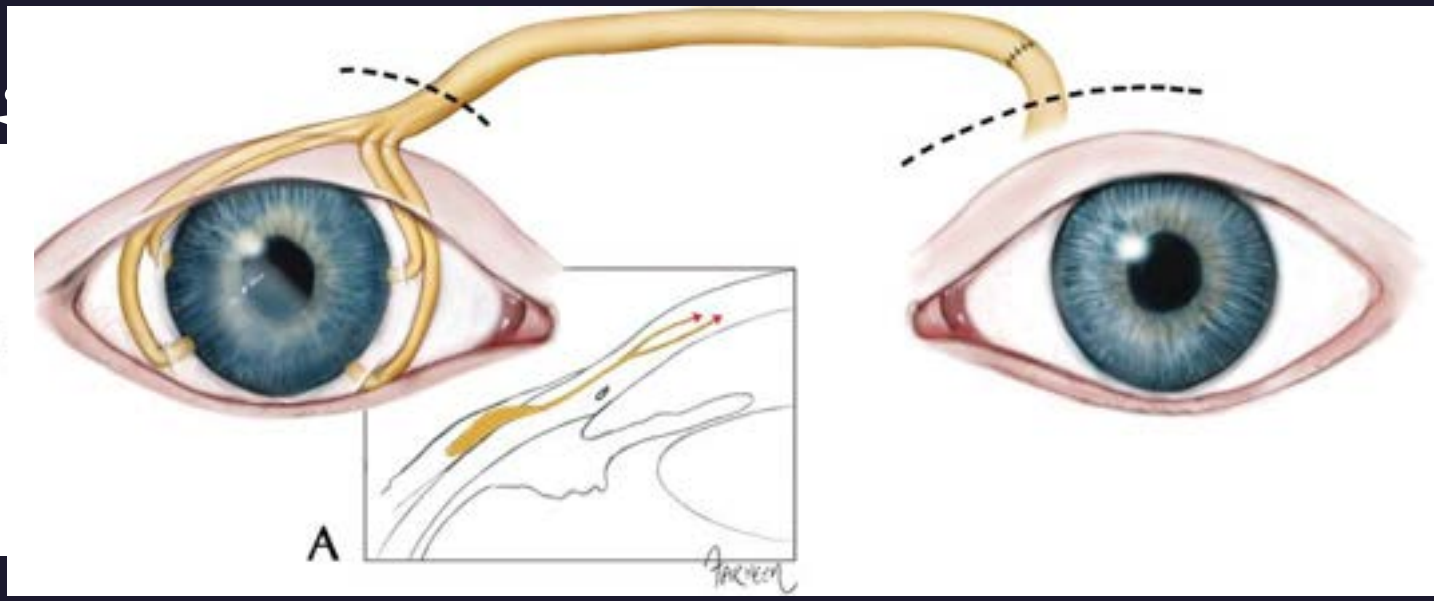


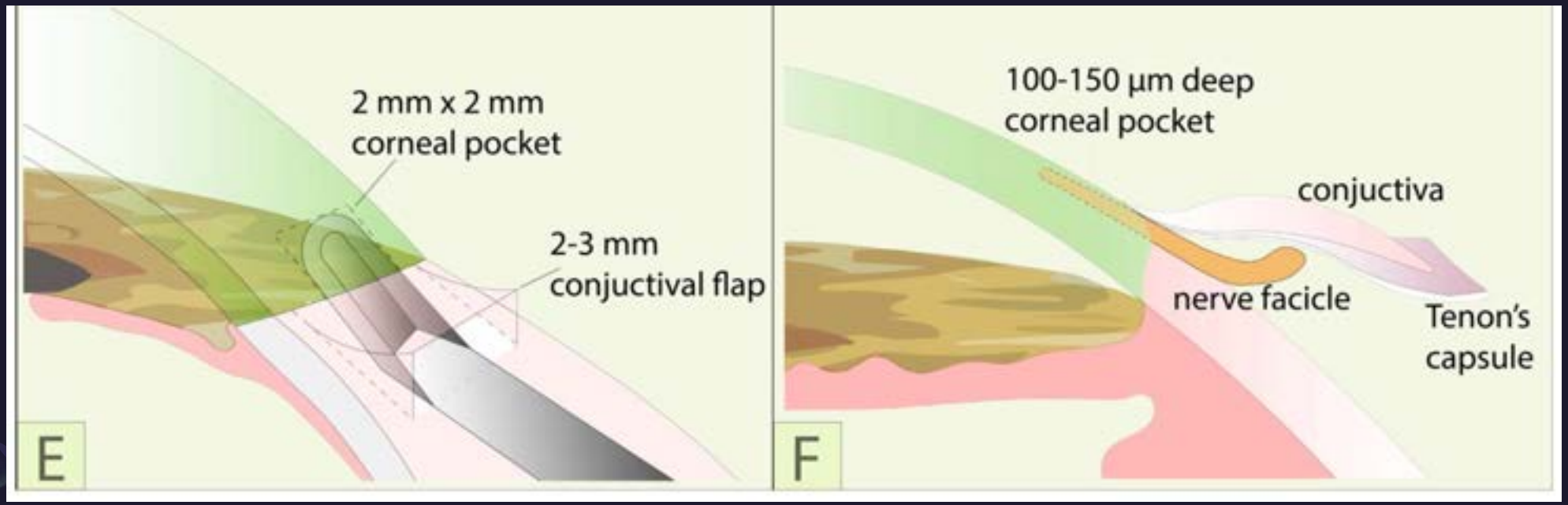
Corneal Neurotizati

> Ophthalmic Plast Reconstr Surg. 2019 Mar/Apr;35(2):133-140.
doi: 10.1097/IOP.0000000000001181.

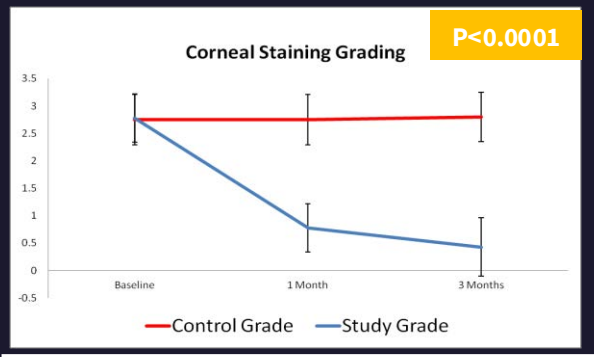
Minimally Invasive Corneal Neurotization With Acellular Nerve Allograft: Surgical Technique and Clinical Outcomes

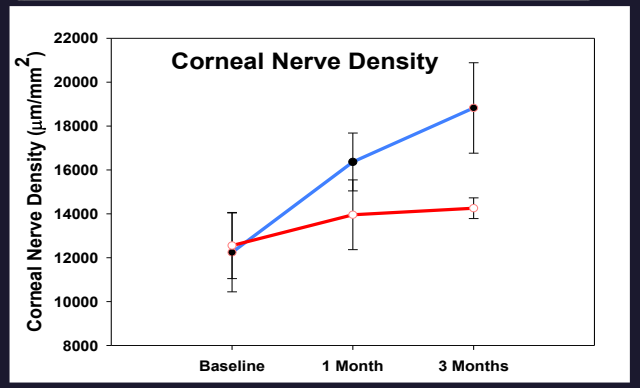
Ilya M Leyngold [1], Michael T Yen [2], James Tian [3], Mark M Leyngold [4], Gargi K Vora [5], Christopher Weller [6]

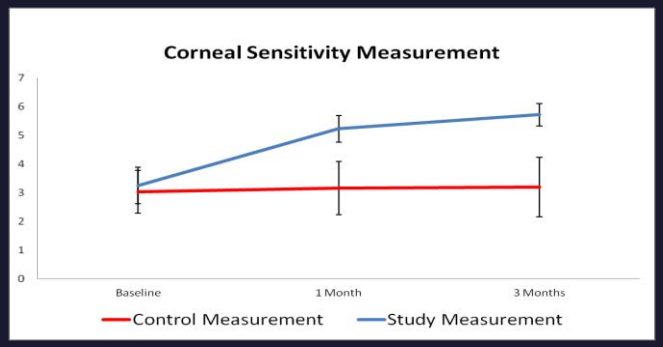


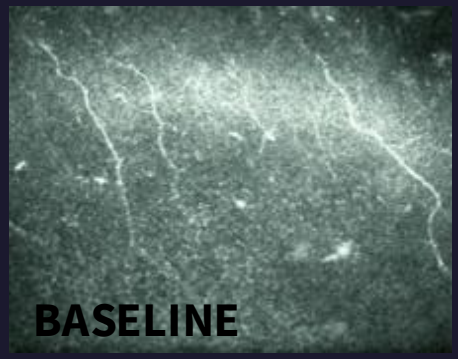


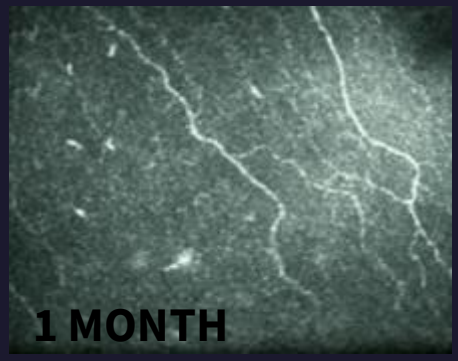
Corneal Nerve Regeneration in Dry Eye

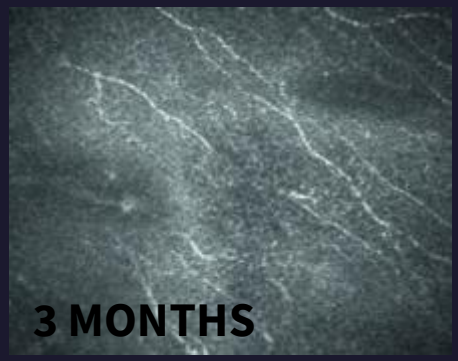












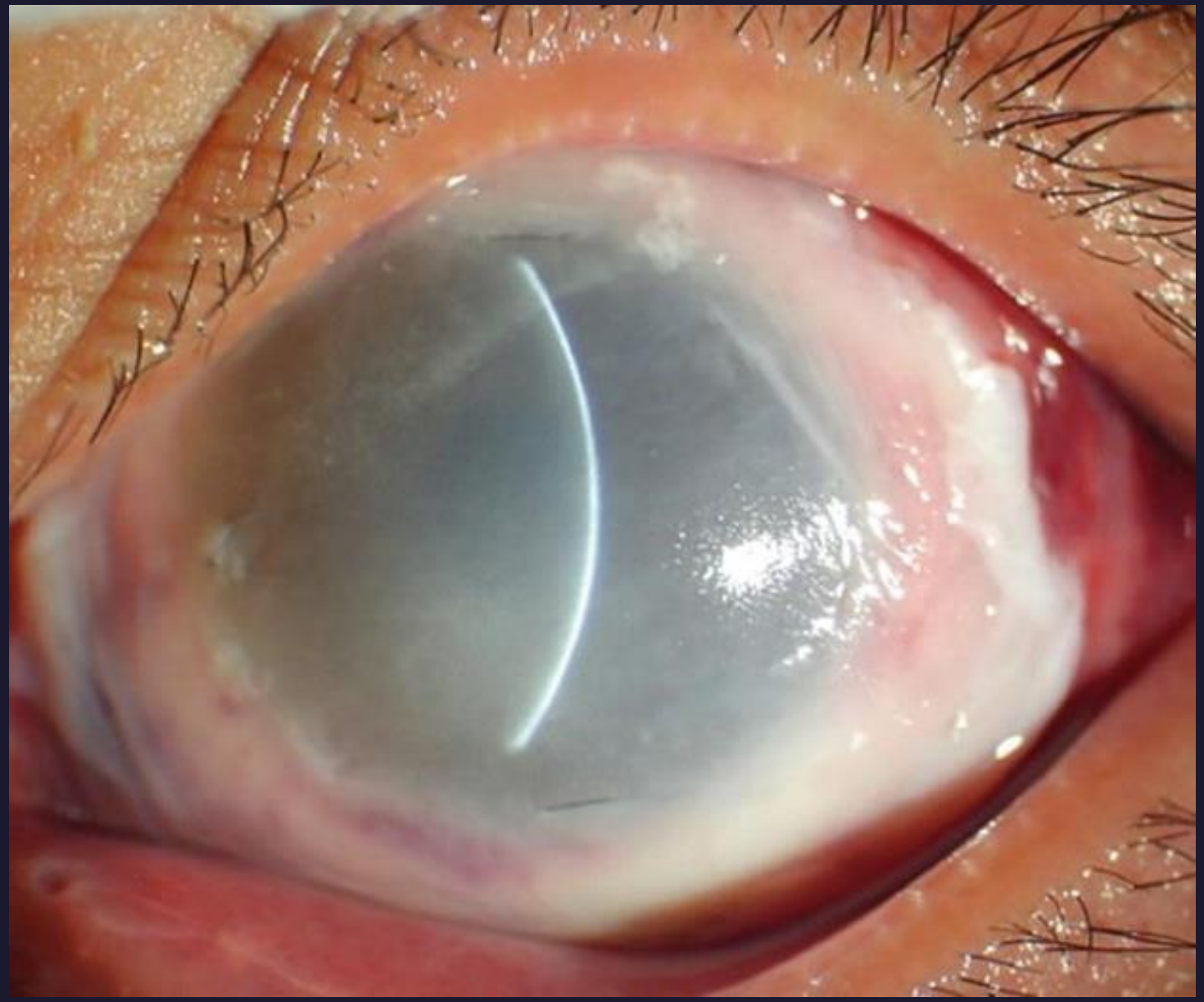
John, T, Tighe, S, Sheha, H. et al. Corneal Nerve Regeneration after Self-Retained Cryopreserved Amniotic Membrane in Dry Eye Disease. *J Ophthalmol*. 2017;2017:6404918.

Clinical Indications

- Neurotrophic Keratopathy
- Chemical/Thermal Burns
- Persistent Epithelial Defects
- Severe Dry Eye (especially inflammatory)
- Surgical Indications

Chemical/Thermal Injury

- Protein coagulation/denaturation of cornea
- Limbal ischemia and limbal stem cell damage
- Epithelial defect and corneal haze



Chemical/Thermal Injury

Roper Hall Classification for Ocular Surface Burns			
Grade	**Prognosis**	**Cornea**	**Conjunctiva/Limbus**
I	Good	Corneal epithelial damage	No limbal ischemia
II	Good	Corneal haze, iris details visible	<1/3 limbal ischemia
III	Guarded	Total epithelial loss, stromal haze, iris details obscured	1/3-1/2 limbal ischemia
IV	Poor	Cornea opaque, iris and pupil obscured	>1/2 limbal ischemia

- Lubrication, cycloplegia
- Topical steroid and antibiotic
- Doxycycline and Vitamin C
- Amniotic membrane

Chemical/Thermal Injury

> Ophthalmology. 2025 Feb;132(2):154-163. doi: 10.1016/j.ophtha.2024.08.021. Epub 2024 Oct 10.

Efficacy of Amniotic Membrane Grafting for the Treatment of Chemical and Thermal Ocular Surface Injuries: A Report by the American Academy of Ophthalmology

Peter B Veldman [1], Mark A Greiner [2], Maria S Cortina [3], Anthony N Kuo [4], Jennifer Y Li [5], Darby D Miller [6], Roni M Shtein [7], Mitchell P Weikert [8], Jia Yin [9], Stephen J Kim [10], Joanne F Shen [11]

- Amniotic membrane grafting significantly improved corneal re-epithelialization in eyes with moderate-grade burns
- For severely burned eyes, AMG demonstrated no advantage over medical therapy

Chemical/Thermal Injury

Randomized Controlled Trial > Am J Ophthalmol. 2019 Mar:199:209-215.
doi: 10.1016/j.ajo.2018.11.001. Epub 2018 Nov 10.

Amniotic Membrane Transplantation in Acute Severe Ocular Chemical Injury: A Randomized Clinical Trial

Medi Eslani [1], Alireza Baradaran-Rafii [2], Albert Y Cheung [3], Khaliq H Kurji [3], Hamidreza Hasani [2], Ali R Djalilian [4], Edward J Holland [5]

- 60 patients with grade 4 chemical injury (opaque cornea, >50% limbal ischemia)
- 30 patients received lubrication, steroid, Vitamin C and doxycycline
- 30 patients received that and amniotic membrane
- Epithelial healing the same between groups, 22 eyes without AMG developed central KNV, only 16 eyes with AMG developed central KNV

Clinical Indications

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Persistent Epithelial Defect

- After corneal ulcer
- In limbal stem cell deficiency
- In cornea structural conditions
- With ocular inflammation
- Post-surgical
- Neurotrophic keratitis

Persistent Epithelial Defect

Clinical Outcomes of In-office Sutureless Amniotic Membrane Transplantation in Persistent Epithelial Defect

Choong Man Choi[1], Hyun Sun Jeon[1,2]

- Retrospective, small sample size of 9 patients with neurotrophic keratopathy, infectious keratitis, LSCD, or marginal keratitis treated with amniotic membrane
- **77.8% success rate** per patient (failures due to AMT displacement and uncontrolled infection)

Persistent Epithelial Defect

Sutureless Amniotic Membrane ProKera for Ocular Surface Disorders: Short-Term Results

Kunal Suri, M.D., Mustafa Kosker, M.D., Irving M. Raber, M.D., Kristin M. Hammersmith, M.D., Parveen K. Nagra, M.D., Brandon D. Ayres, M.D., Colleen P. Halfpenny, M.D., and Christopher J. Rapuano, M.D.

- Retrospective study of 35 eyes from 2008-2012
- Group 1: Infectious keratitis (44% success)
- Group 2: Neurotrophic keratopathy (64% success)
- Group 3: Chemical injury (80% success)
- Group 4: Other (70% success)
- **Only 17% with discomfort**

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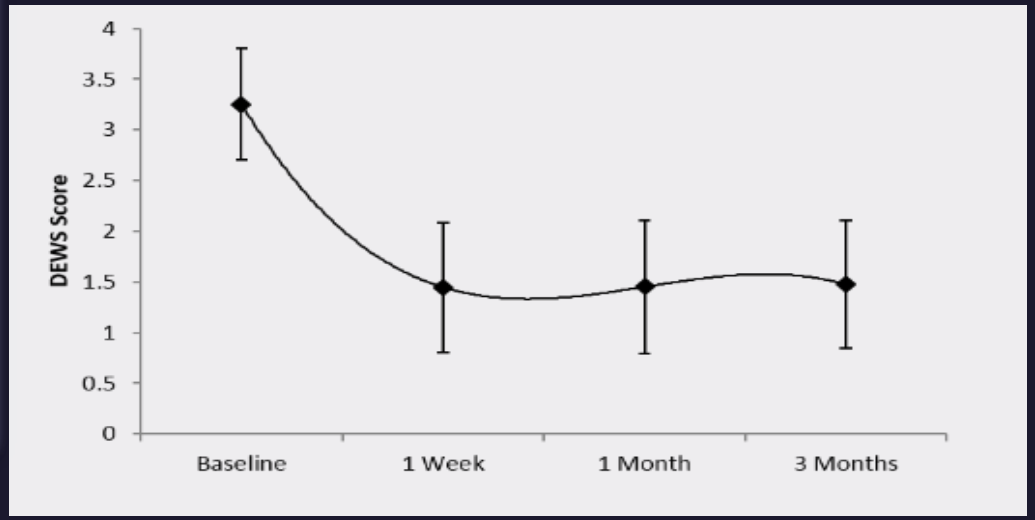
Verification of Lasting Benefit in Dry Eye

- **A total of 97 eyes of 84 patients**: 12 (14%) male, 69 (82%) Female with severe dry eye (DEWS 3-4) despite maximal medical treatments
- Manifested with superficial punctate keratitis (86%), filamentary keratitis (13%), exposure keratitis (19%), neurotrophic keratitis (2%), and corneal epithelial defect (7%).
- After Cryopreserved AM (Prokera) placement for **5.4 ± 2.8 days**, **74 (88%)** patients demonstrated notable improvement of DED symptoms, improved ocular surface, and notable reduction of the DED severity **lasting for at least 3 months**.



McDonald, M., Sheha, H., Tighe, S. et al. Treatment outcomes in the DRy Eye Amniotic Membrane (DREAM) study. *Clin Ophthalmol.2018; April 9*:12:677-681.

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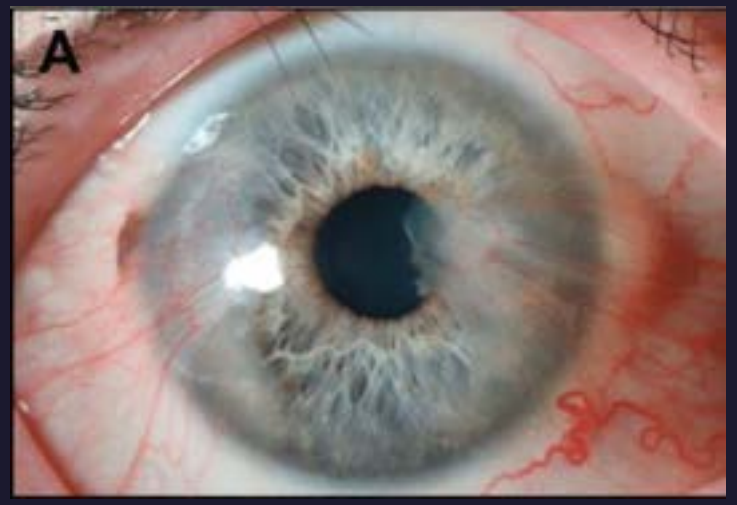
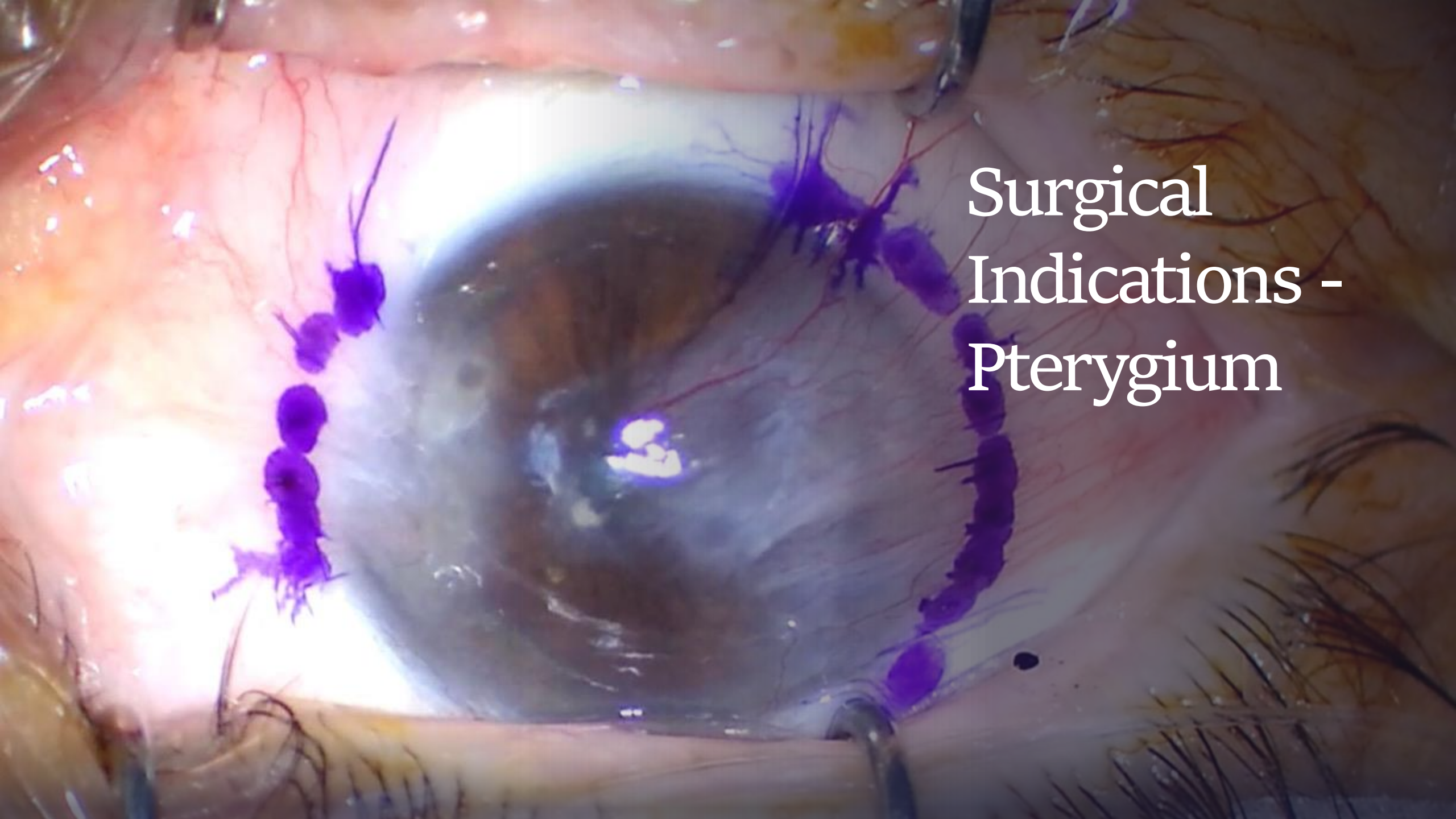
Surgical Indication

- **Conjunctiva**
  - **Large/Double Pterygium**
  - **Neoplasia Excision**
  - **SJS/TEN**
  - **Symblepharon release**
- **Cornea**
  - **Superficial keratectomy**

Surgical Indications - Conjunctiva

- Used as **Graft** to enhance epithelization
- Pterygium
  - **Useful in large/double pterygia** when not enough conjunctiva for autograft
- Neoplasia
  - AMT, particularly when used as a combination/Sandwich, has been shown to **re-epithelize faster** and **have lower tumor recurrence rates**
- Stevens Johnson Syndrome
  - Helps provide growth of healthy conjunctiva and reduce cicatricial scars





Surgical Indications - Pterygium

Surgical Indications – Superficial Keratectomy

Head-to Head Comparison Review

"A Comparison of CAM and BCLs in their ability to provide high-quality healing after a Superficial Keratectomy"

- Neel R. Desai, MD

10 Patients with Bilateral Basement Membrane Dystrophies had an SK performed on each eye followed by:

- **BCL placed** on eye with the less severe disease (Control Group)
- **PKS placed** on eye with the more severe disease (Study Group)

*Both treatment groups received the same regimen of topical drops.

	Number of Eyes Treated	
	BCL Results	CAM
Complete Re-Epithelialization at Day-5	2	7
Complete Re-Epithelialization at Day-7	5	8
Trace or Worse Residual Haze/Scarring at Day-7	10	1
Trace or Worse Residual Haze/Scarring at Day-30	10	2
Net Change in Snellen Visual Acuity at Day-30	-2	2
Comparison of Pain Scores	No Statistical difference	

Surgical Indications – Superficial Keratectomy

- Video

Amniotic Membrane Placement Technique

- Video

High Yield Review

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Thank You!

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- Personal cell: 727-239-6808

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