

AMNIOTIC MEMBRANE USES IN OPTOMETRY

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DR. STEPHANIE WOO'S FINANCIAL DISCLOSURES

- I have received honorarium from the following companies:
 - Alcon
 - Specialeyes
 - X-cel Contacts
 - Essilor
 - Visionary Optics
 - Blandhard Contacts
 - Bausch and Lomb
 - Biotissue
 - Shire
 - Art Optical
 - Contamac
 - Scleral Lens Education Society
 - STAPLE program
 - GPLI

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EXPECTED LEARNING OBJECTIVES

- Needs assessment statement:
 - To enable practitioners to comfortably use amniotic membranes within their scope of practice.
- At the end of the session, attendees should be able to:
 - Identify 3 good candidates for an amniotic membrane
 - Describe 2 differences between dehydrated and wet tissue
 - Explain 2 diagnoses that may benefit from an amniotic membrane
 - Properly bill for amniotic membrane therapy

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RARE CORNEAL ULCER

- Patient presented to the clinic with THIS!



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WHAT IS THIS?

- Bacteria
- Fungus
- Virus
- Amoeba
- Corneal Plaque



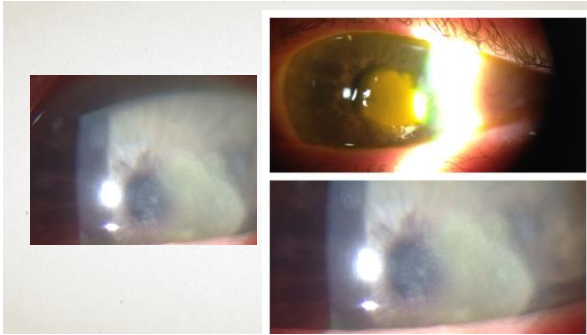
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REVIEW PAST AND CURRENT TREATMENT

- Finally was fit with an amniotic membrane when all else failed.



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WHAT IS AN AMNIOTIC MEMBRANE?

- Amniotic membranes are derived from placentas
- The amniotic membrane (AM) is the inner layer of the fetal membranes and consist of 3 different layers: the epithelium, basement membrane and stroma which further consists of three distinct layers: the inner compact layer, middle fibroblast layer and the outermost spongy layer

Chinnam, M et al. Human amniotic membrane transplantation: Different modalities of its use in ophthalmology. World J transplant. 2014 Jun 24;4(2):111-21

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WHAT DOES THE AMNIOTIC MEMBRANE DO FOR A DEVELOPING BABY?

- The amnion is a membrane which closely covers the embryo.
- It fills with amniotic fluid which causes the amnion to expand and become the amniotic sac which serves to provide a protective environment for the developing embryo

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HISTORY OF AMNIOTIC MEMBRANE USE

- Natural amniotic membranes have been successfully used for wound and reconstructive purposes since the early 20th century.
- Human amniotic membranes have been proven effective at healing wounds. The mechanism of action is poorly understood.¹
- The growth factors in amniotic tissue are thought to assist in healing.
- Amniotic membrane is rich in collagen and various growth factors that support the healing process
- Improves wound closure and reduces scar formation
- Unique properties include the lack of immunologic markers, conferring an "immune privileged" status on the allografts; antibacterial properties; and the ability to reduce pain on application.²

1. Koob, et al. Cytokines in single layer amnion allografts compared to multilayer amnion/chorion allografts for wound healing. 8 Aug 2014
2. Entwistle, D et al. Scientific and Clinical Support for the Use of Debricated Amniotic Membrane in Wound

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HISTORIC AMNIOTIC MEMBRANE USES:

- The treatment of acute chemical burns
- Surgical dressings
- Reconstruction of the oral cavity, bladder, tympanoplasty, arthroplasty and onfalocoele
- Prevents tissue adhesion in surgery of the head, abdomen, pelvis, vagina and larynx

Young RL et al. The use of an amniotic membrane graft to prevent postoperative adhesions. Fertil Steril 1991. Mar;55(3):624-8

11

Treatment of diabetic foot ulcers

Zelen C. A prospective randomised comparative parallel study of amniotic membrane wound graft in the management of diabetic foot ulcers. International Wound Journal ISSN 1742-4001
Mermel L, Portier N, Sainthillier JM, et al Use of amniotic membrane transplantation in the treatment of venous leg ulcers. Wound Repair Regen 2007;15:459-64

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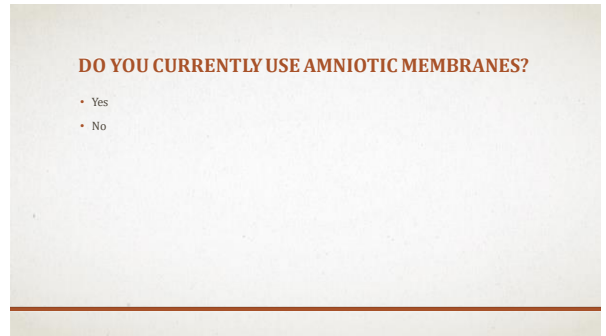
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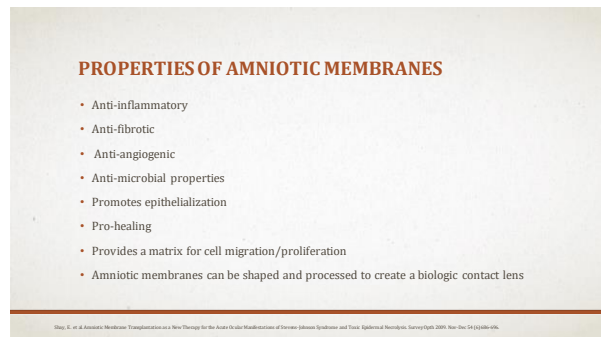
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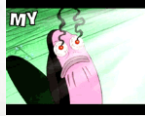
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HOW DID OCULAR AMNIOTIC MEMBRANE USE START?

- The first ocular indication was suggested by deRoeth in 1940 following successful treatment of a chemical burn of the ocular surface.
- It was not until Juan Batlle's report in 1992 that it re-emerged as an important modality of treatment.
- There are over 700 peer-reviewed publications for the ocular use of amniotic membranes highlighting novel increasing indications and therapeutic applications.



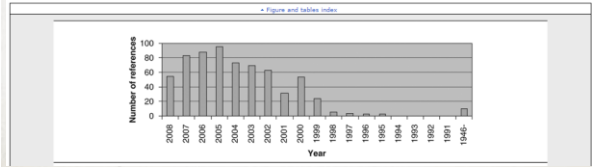
Rahman, I, et al. Amniotic membrane in ophthalmology: indications and limitations. Eye (2009) 23, 1954-1961.

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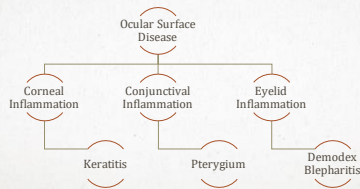
Table 1. To show the increasing number of peer reviewed publications relating to the ocular use of amniotic membrane



Rahman, I, et al. Amniotic membrane in ophthalmology: indications and limitations. Eye (2009) 23, 1954-1961.

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INFLAMMATION IS THE HALLMARK OF ALL OCULAR SURFACE DISEASES



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INFLAMMATION IMPACTS WOUND HEALING

- **Inflammation** the first sign of wound healing
- **Uncontrolled Inflammation** leads to:
 - 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 quality healing and minimize the risk of scar / haze

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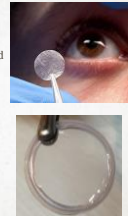
DIFFERENCES BETWEEN DRY AND WET



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AMNIOTIC MEMBRANE OPTIONS: DRY OR WET

- Dry amniotic membranes are dehydrated in a way that preserves the key elements associated with healing.
- The sterilized tissue is packaged and stored at room temperature and has a 4-5 year shelf life (varies by manufacturer).
- Wet amniotic membranes are made by clipping a piece of amniotic membrane tissue in between two rings made out of a clear, flexible material.
- Wet amniotic membranes are cryo-preserved
- Wet amniotic membranes are stored in a glycerol media (to prevent freezing)
- Stored between 33 -50 degrees F = shelf life 3 months
 - 32 -(-)47 F (freezer) = shelf life 1 year




Adida, P, et al. Amniotic membrane grafts: "Dry" or "Wet"? A clinical and histologic comparison. Ophthalmol. 2001 Aug; 108(8): 145-147. [http://dx.doi.org/10.1016/S0014-3989\(01\)05811-9](http://dx.doi.org/10.1016/S0014-3989(01)05811-9)

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DRY (DEHYDRATED) AMNIOTIC TISSUE

- Each company uses a proprietary process
- Dehydrated
- Some are terminally sterilized
- Retained biostructure, proteins, cytokines



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AMBIODISK

AmbioDisk™ Specifications
 AmbioDisk™ is a processed, dehydrated, sterilized human amniotic membrane allograft.

Human amniotic membrane is a unique collagenous membrane derived from the placenta, the area in which the human fetus grows and develops within the mother's uterus. Human amniotic membrane is composed of multiple layers.


AmbioDisk™ is a minimally manipulated, dehydrated, non-viable cellular amniotic membrane allograft that contains multiple extracellular matrix proteins, growth factors, cytokines and other specialty proteins present in amniotic tissue to provide a barrier membrane that enhances healing.

AmbioDisk™ allografts are human tissue products and appearance may vary between donors. Variations in color (tan to light brown), opacity, and thickness are normal due to the nature of human tissue.

Two sides: One with the stromal matrix and the other with the basement membrane.

Orient the graft with the "IOP" watermark facing the physician to ensure that the stromal side is making contact with the eye.

The basement membrane side is face up in the packaging.



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Bio D Optix

Has a "dull" side and a shiny side.

Identify the dull side - that is the side that should make contact with the cornea.

The shiny side should face practitioner.

PERFORMANCE

- Dehydrated using our proprietary "DryFlow" process that preserves the inherent ECM, growth factors, and cytokines of the amniotic tissue
- Easy to apply and conforms well to the anterior ocular surface
- Placement generally does not require sutures or glue


CONVENIENCE

- Circular or rectangular sizes for appropriate fit
- Dehydrated product allows for easy fit for size fitting
- Room temperature storage until to use and shelf
- Convenient for use in inpatient, outpatient or clinic settings

COMPLIANCE

- Amniotic tissues have been identified as immune privileged because they rarely evoke an immune response in their natural location
- Tissues recovered from low, healthy donors during cesarean deliveries
- Critical selection, tissue screening and processing minimize and preclude most or second all applicable industry standards to ensure patient safety

Common Clinical Applications of Amniotic Tissues	Product ID	SIZE
• Eyelid Swelling	• Permanent Epithelial Contact	OK-010012 1.5 x 2.0cm
• Membrane Opacities	• Ptosis	OK-010013 2.0 x 2.0cm
• Ptosis	• Band Keratopathy	OK-010009 2.0 x 2.0cm
• Corneal Cloud	• Ocular Herpesopathy	OK-010011 2.0 x 2.0cm
• Recurrent Corneal Erosion		OK-010015 15.0cm x 15.0cm (dog)



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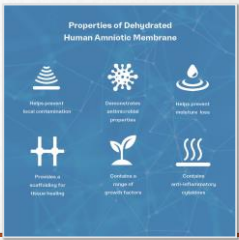
The science behind Avenova Allograft

The intrinsic properties of the dehydrated human amniotic membrane (DHAM) make AVENOVA ALLOGRAFT a versatile option for a wide variety of topical covering applications

- Consists of only the amnion layer of the placental membrane (20 – 50 microns thick)
- Ideal for delicate ophthalmic applications
- Can be applied directly to the eye without the use of additional hardware or sutures
- Has no orientation issues - can be placed with either side facing down
- Is aseptically processed and terminally sterilized via e-beam irradiation
- Has a 4-year shelf life and can be stored at ambient temperatures

Properties of Dehydrated Human Amniotic Membrane

- Highly resistant to bacterial contamination
- Dehydrated to preserve natural properties
- Highly resistant to chemical agents
- Promotes a scaffold for tissue healing
- Contains a variety of growth factors
- Contains anti-infective capabilities



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DRY VS. WET

<p>PROS OF DRY</p> <ul style="list-style-type: none"> • Cheaper for practitioner • Easy storage • Long shelf life • More comfortable for the patient 	<p>PROS OF WET</p> <ul style="list-style-type: none"> • May retain more of the innate characteristics of the natural amnion, resulting in potentially better outcomes • Cryopreserved • Cryopreserved amniotic membrane is the only tissue cleared for wound healing by the FDA • Keeping extracellular matrix intact helps to regulate and promote tissue regeneration¹
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1. Jin CZ, et al. *Tissue Eng.* 2007; 13:693-702

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DRY VS. WET

<p>CONS OF DRY</p> <ul style="list-style-type: none"> • May not retain all of the characteristics of the natural amnion • Dehydrated amniotic membranes contains may only trace amounts of HC-HA and PTX3, which may be essential for regenerative wound healing and controlling inflammation 	<p>CONS OF WET</p> <ul style="list-style-type: none"> • Shorter shelf life • More costly to the practitioner • Must store in refrigerator or freezer • May be more uncomfortable due to the plastic ring (1.6.5mm diameter)
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RISKS OF AMNIOTIC

- Amniotic membranes are heavily syphilis
 - Quality control from FDA
- Tight contact lens can cause inc
- Some risk for calcifications with

British Journal of Ophthalmology

Corneal calcification after amniotic membrane transplantation

Abstract

Background: Amniotic membrane transplantation (AMT) has become well established as a treatment for chronic epithelial defects, conjunctival reconstruction, and partial lamellar cell deficiency. The aim of this study was to describe cases of corneal calcification following AMT and to search for risk factors that might predispose to this unusual finding.

Methods: Details of 117 AMTs on 93 corneas of 91 patients with a follow-up period of at least 1 month performed since 2009 were collected prospectively. In those with calcification clinical photographs were studied and the medical records retrospectively examined.

Results: 15 calcifications in 117 AMTs (12.8%) were identified, occurring 3–17 (median 6.1) weeks after AMT, during a follow-up period of 4–21 (median 25) weeks. Overall epithelial healing rate was 83%. Calcifications covered a surface area between 0.7–49.5 mm² (median 5.5 mm²) with varied morphology. The

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SO WHICH IS BETTER – WET OR DRY?

- There is no right or wrong answer.
- Depends on the practitioner, the patient, and condition being treated.
- Personally, I have success with both products.

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ESSENTIALLY, AMNIOTIC MEMBRANES CAN OFFER:

- Quicker healing
- Less pain
- Less scarring
- Less inflammation

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POLL: WHICH PATIENT WOULD LIKELY NOT BENEFIT FROM AN AMNIOTIC MEMBRANE?

- Active herpes simplex keratitis
- Dry eye disease
- Corneal ulcer
- Corneal scar from trauma
- Unresolved SPK from PRK surgery 4 days ago

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AMNIOTIC MEMBRANES HAVE A HUGE ROLE IN THE OCULAR WORLD

- Uses in ocular surgeries:
 - Corneal defects
 - Partial stem cell deficiency
 - Chemical burns
 - Conjunctival surgery
 - Pterygium surgery
 - Symblepharon
 - High risk corneal transplants
 - Other corneal surgeries

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AMNIOTIC MEMBRANE USES IN OPTOMETRY

- Stevens-Johnson
- Shield ulcers
- Corneal abrasions
- Corneal ulcers
- Corneal burns
- Filamentary keratitis
- Dry eye and exposure keratopathy
- Recurrent corneal erosion
- Salzmann's nodular degeneration
- Herpes keratitis

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BANDAGE MEMBRANE

- Many of our problems.
- Commonly seen
- How do bandage
- Review of Op (Prokera)

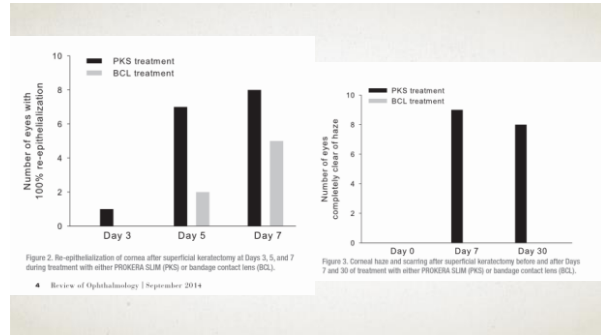
Sponsored By
biotissue

A comparison of cryopreserved amniotic membrane and bandage contact lens in their ability to provide high-quality healing after superficial keratectomy

Neel R. Desai, MD, The Eye Institute of West Florida

ABSTRACT
Purpose: To compare self-retained cryopreserved amniotic membrane, PROKERA[®] SLIM, with bandage contact lens in corneal wound healing.
Methods: Superficial keratectomy was performed on all eyes. The epithelialization of corneal wounds faster than with BCL. In a net gain of 2 lines of best corrected visual acuity (BCVA) compared with a net loss of BCVA with BCL at day 30, and in wound healing without sub-epithelial hazing or scarring. These results were seen with PK. These the desire to prevent and treat inflammation and scarring while simultaneously promoting rapid healing. It is well understood that the adult healing process is initiated and then dominated by an often intense inflammatory response that ultimately leads to

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SUPPLIES NEEDED/ INSERTION PROCESS

DRY

- Supplies:
 - Traditional bandage lens
 - Dehydrated amniotic membrane (cut to about 5-15mm diameter circle)
 - Pledget to press materials together
 - Saline
- Inserted like a bandage contact lens
- Can also use lid speculum

WET

- Supplies:
 - Gloves
 - Sterile saline
 - Topical numbing drops
 - Eye patching materials
- Inserted under the upper lid first, then the lower lid

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PREPARING DEHYDRATED AMNIOTIC MEMBRANE

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PREPARING DEHYDRATED MEMBRANE OPTION 2

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PREPARING WET AMNIOTIC MEMBRANE



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AFTER INSERTION

- It is up to the doctor if they want the patient to use eye drops during this time (can be an excellent drug delivery device!)
- See the patient back for follow ups according to pathology:
 - Dry eye vs severe corneal burn

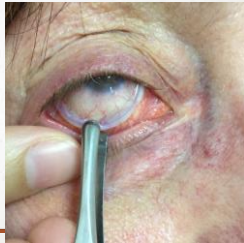
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REMOVAL

- Dry: Remove similar to bandage contact lens



- Wet: use topical numbing agent and forceps



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REIMBURSEMENT

- Proper code is 65778 (*Placement of amniotic membrane on the ocular surface for wound healing; self-retaining*)
- 0 day global period
- How much is the cost of an amniotic membrane to me as the practitioner?
 - Ranges from \$100-\$1000 per device, depending on the type and the amount purchased
- *IMPORTANT NOTE: THERE IS A MEDICARE CARRIER IN ANOTHER STATE THAT ONLY RECOGNIZES THE CRYO-PRESERVED AMNIOTIC MEMBRANE FOR 65778

As of July, 2018

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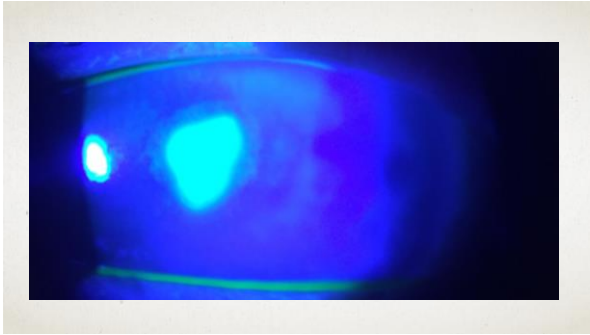
CASE REPORTS OF COMMON CORNEAL ETIOLOGIES

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BB 54 YO WHITE FEMALE

- Presented to the clinic complaining of "white spot" on OS
- Onset 2 days ago
- Watery, photophobia, redness
- Currently wears Acuvue 2 - sometimes sleeps in lenses
- Has not worn CLs in 2 days

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TREATMENT AND PLAN

- Large central corneal ulcer or abrasion without hypopyon
- Treatment: Fortified tobramycin Q1hr and Vigamox Q1 hr. Ambiodisk placed today. RTC 24 hour follow up

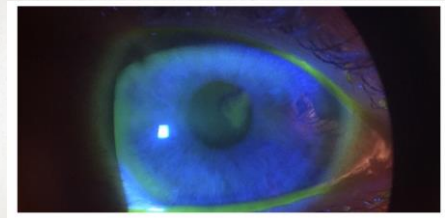
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1 DAY FOLLOW UP

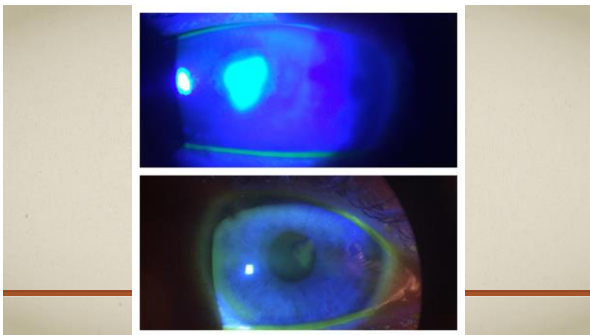
- Ulcer had decreased in size
- Less microcystic edema
- Plan: Continue fortified Tobramycin Q1hr and Vigamox Q1hr and Ambiodisk remains. RTC 24 hours
- Patient followed up every 24 hours for the first 4 days, then every 48 hours for next week
- Each day there was an improvement in OS ulcer

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After 2 weeks



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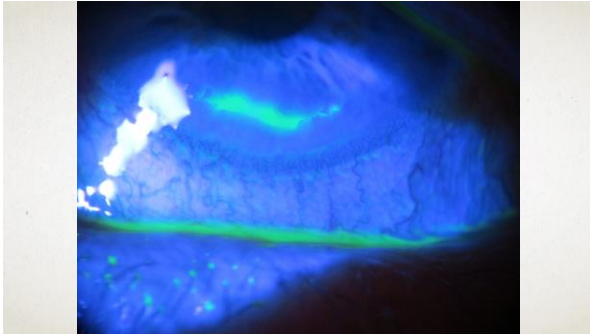


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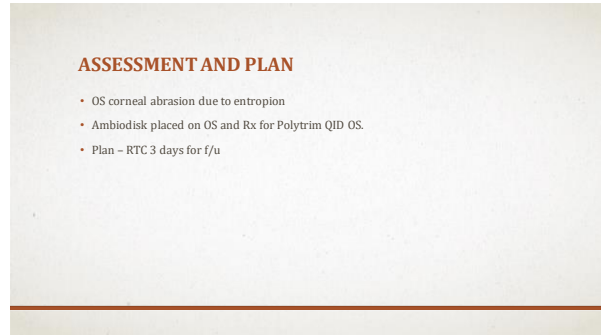
FW 66 YEAR OLD WHITE MALE

- Presented to the clinic with complaints of a watery, red OS for 2 days. Does not recall getting anything in his eye. No significant ocular history.
- No complaints of the OD

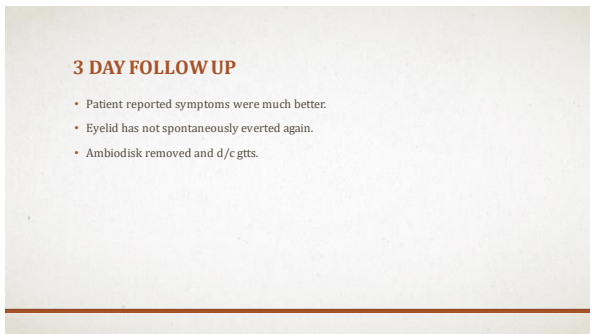
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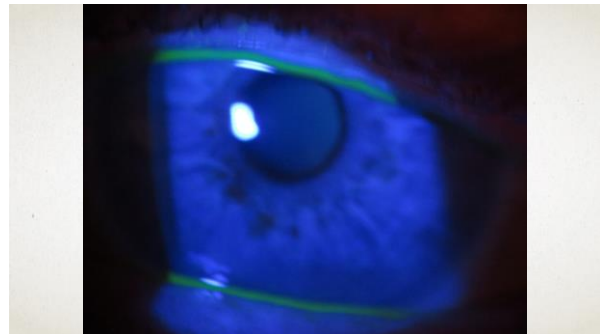
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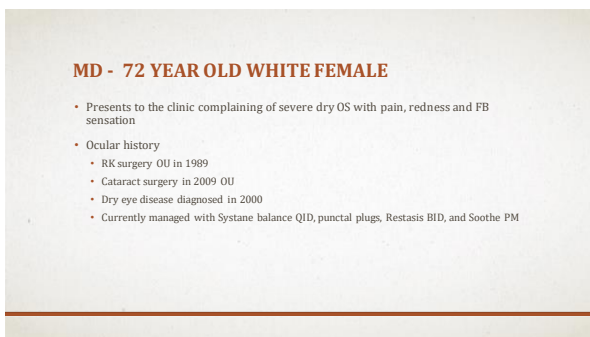
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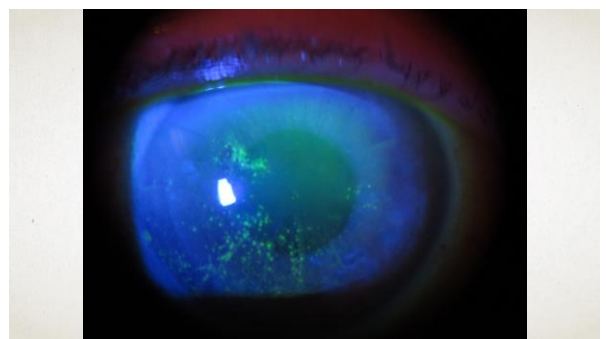
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ASSESSMENT AND PLAN

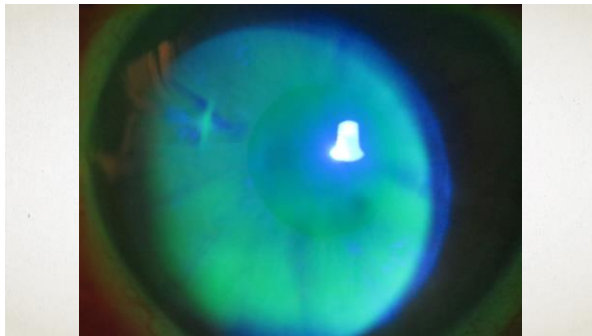
- Dense SPK due to dry eye disease and K-sicca (OS> OD)
- Ophthalmologic Eclipse lens placed today and continue Systane Balance QID, Restasis BID, and Soothe PM
- RTC 1 week f/u

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1 WEEK FOLLOW UP

- States symptoms are much improved in the OS
- Using all gts and gel as directed

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DISCUSSION

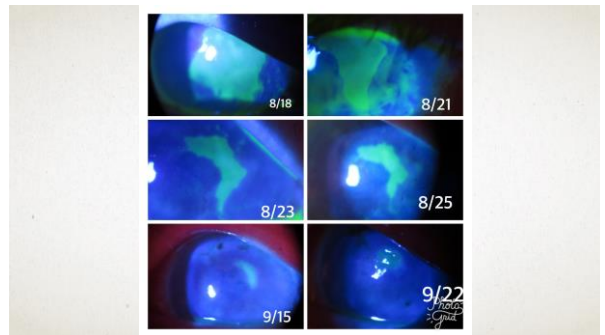
- This patient has a chronic condition and is frequently seen for management of dry eye disease.
- Her SPK returns often, and we will place another amniotic membrane on the affected eye as needed.
- She has been fit into scleral lenses, which alleviate some of the dry eye signs/symptoms (when she wears them)

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RF - 68 YO WHITE MALE

- Presents to the clinic with a red, burning painful eye that he woke up with.
- Ocular history is positive for LASIK OU
- Upon slit lamp, found a large epithelial defect secondary to dry eye.
- Was not responsive to bandage contact lens, artificial tears and gels
- 1 week later = Plan = place Prokera along with Vigamox q1hr WA and f/u 24 hours.
- Each day/week there was an improvement

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DN case: Bandage contact lens vs amniotic membrane

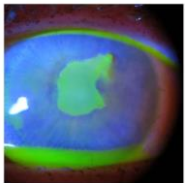
DN 63 year old female

Presents to clinic with extreme eye pain OS
Wears Night and Day lenses Continuous
Wear +5.00 OU

Woke up in extreme pain with redness,
Photophobia, and FB sensation

20/LP OS

A/P: Large central ulcer/abrasion. Recommend
Amniotic membrane to speed up healing time
And reduce potential for scarring. Pt refused
Due to cost. Fortified gentimycin Q1h and fortified
Vancomycin Q1hr. RTC 24 hours



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24 HOUR FOLLOW UP

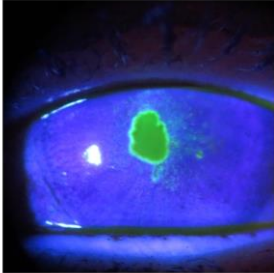
- Pt had been using gtts as directed
- Pain is less severe
- FB sensation improved slightly
- Ulcer/abrasion appears improved from yesterday
- Plan: continue gtts as directed and RTC 24 hours



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24 HOURS LATER

- Pt has been compliant with gtts
- VA is 20/200 today
- Pain is less severe, redness has decreased
- Ulcer/abrasion decreased in size with regular borders
- Plan: continue gtts and RTC 24 hours



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24 HOURS LATER

- Reports compliance with gtts
- Decreased pain
- VA 20/200
- Ulcer/abrasion decreased in size

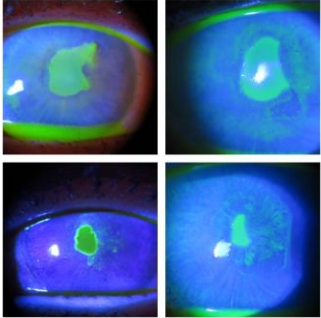


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DN FOLLOW UPS

- BCL was placed after about 8 days of f/u care
- Epithelium finally healed, but dense scar remained
- Started pred forte QID for 2 weeks, then slowly tapered
- Corneal haze remains

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DISCUSSION

- Would an amniotic membrane help to decrease scarring potential?

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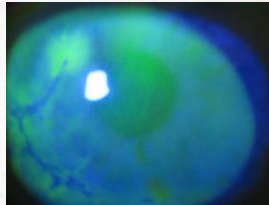
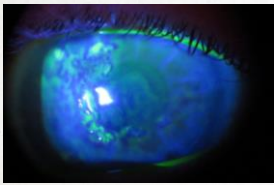
HB 44 YEAR OLD WHITE FEMALE

- Active herpes simplex OD
- Taking oral acyclovir 800 mg 5x/day
- Currently on Viroptic 9x/day
- Corneal specialist referred for biologic bandage insertion

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Before

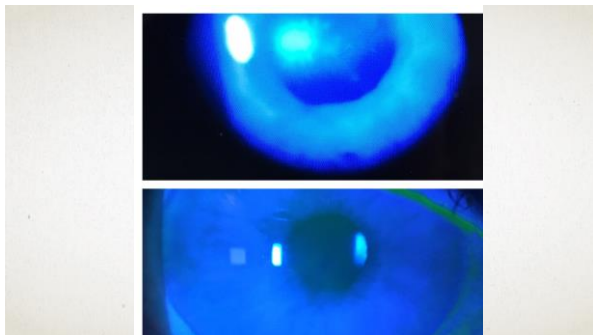
After (1 week)



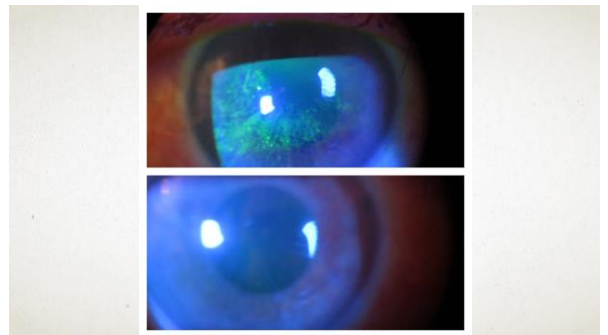
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BEFORE/AFTER PHOTOS

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BIOLOGIC BANDAGES DON'T ALWAYS WORK...

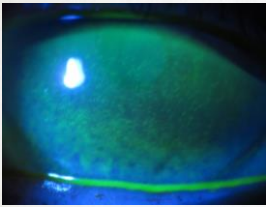
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MM - 67 YEAR OLD WHITE FEMALE

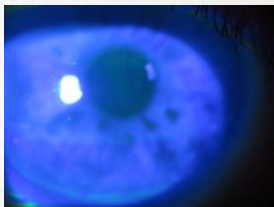
- Chronic dry eye patient, consistently managed with artificial tears, Restasis, punctal plugs, gels, etc.
- Explained option of biological bandage lens, patient opted to try it

80

Before

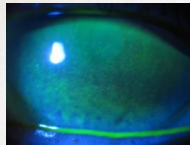


After (1 week)

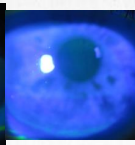


81

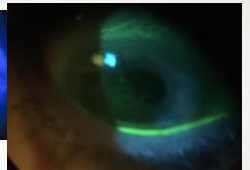
Before



(1 week)



(1 month)



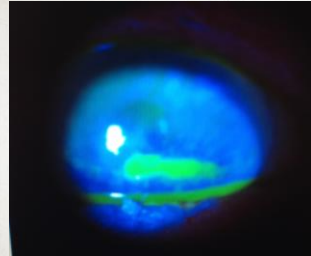
82

GT - 87 YEAR OLD WHITE MALE

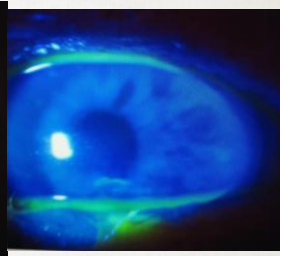
- Presented with FB sensation OD
- Constant for years
- Has been managed with many different drops
- Snowbird (first time to my clinic)

83

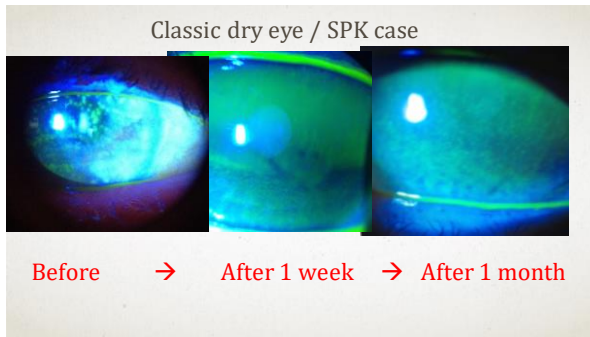
BEFORE



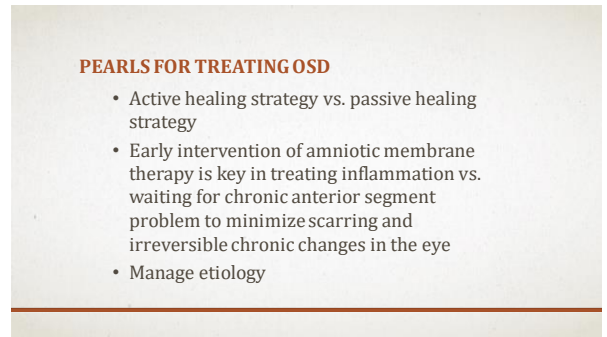
AFTER (1 week)



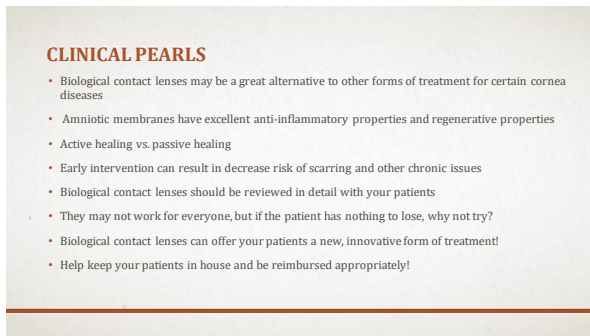
84



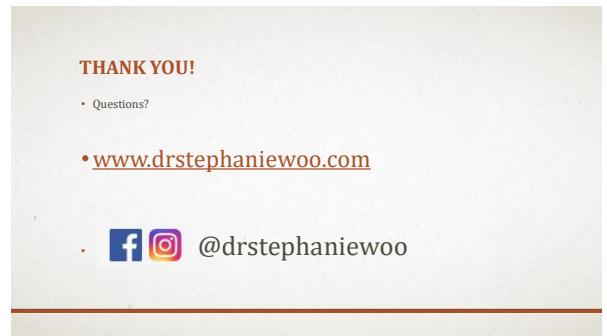
85



86



87



88