



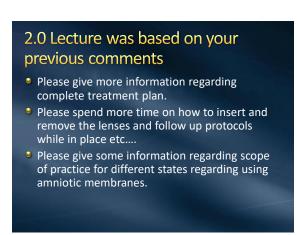








2.0 Lecture was based on your previous comments Please add more detailed information on the course of how and when to follow up with these patients Please explain what we will see clinically during the process of treatment/follow up. Please speak of details of treating bilateral conditions, max length of wearing time? Evidence of how beneficial this is







What is the Amniotic membrane

- Thin but tough transparent pair of membranes, which hold a developing embryo (and later fetus) until shortly before birth.
- The primary function of the amniotic membrane is to protect the fetus from injury.
 - 1. Anti-inflammatory
 - 2. Anti-scarring
 - 3. Anti-angiogenic



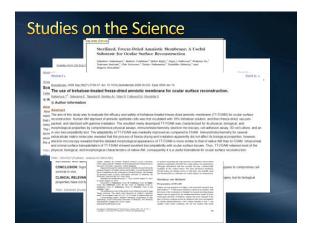
Amniotic membrane

- Amnion is avascular and a translucent membrane composed of an inner layer of epithelial cells which are planted on a basement membrane
- Amnion is made of Collagen I, III, IV, V and VII, laminin and fibronectin of which IV, VII, laminin and fibronectin are also found in conjunctiva and cornea













Prokera

- Approved by FDA Dec 2003 as a Class II medical device comprised of cryopreserved amniotic membrane graft fastened to thermoplastic ring-set
 - Launched in April 2005
 - 17,000 milestone in September 2014
- Dual action promotes healing of ocular surface and controls inflammation
- Stored in medium made of Dulbecco's Modified Eagle Medium / Glycerol containing Ciprofloxacin and Amphotericin B
 - Do not use on patients with a history of drug Rxn to Cipro or amphotericin B

Prokera

- Cryopreserved
- Store in refrigerator x 3 months 1° C to 10° C (33.8° F to 50°F)
- Store in freezer
 - 1 year between -49° C to 0° C (-56.2° F to 32° F)
 - 2 years between -85° C to -50° C (-121° F to -58° F)
- Shelf life is 2 years from date of manufacturer
- Allow to thaw to room temperature unopened for 5-10 min
- Open inner pouch and keep in tray to irrigate
- Rinse with BSS / saline to reduce stinging sensation
- Do not leave in eye longer than 30 days

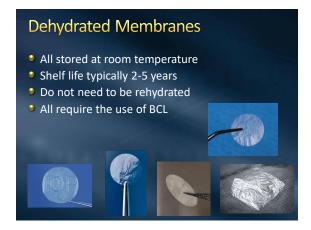


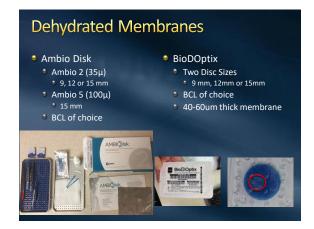


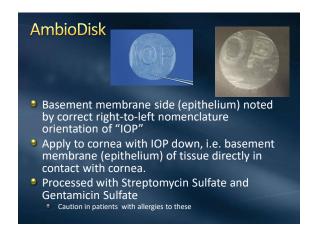


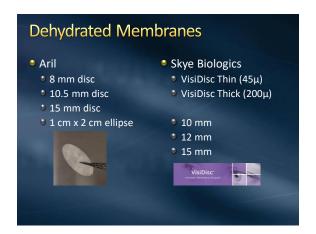


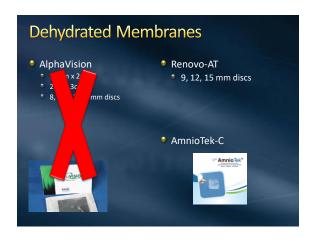
AmbioDisk (IOP Inc. / Katena)
BioDOptix (BioDLogics)
Aril (Seed Biotech)
VisiDisc (Skye Biologics)
AlphaVision (Amniotic Therapics)
ReNovaAT (RegenMed)
AmnioTek-C (ISPP Surgical LLC)





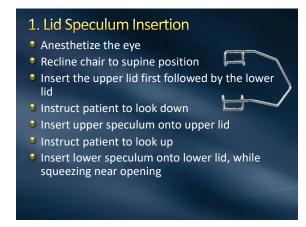








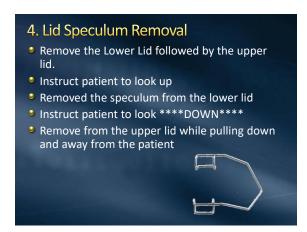






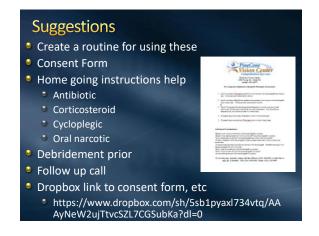


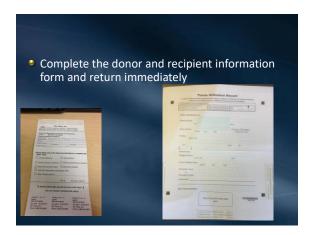








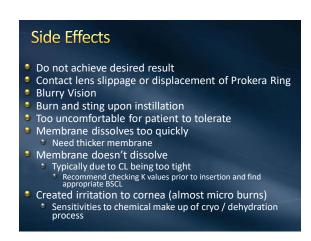




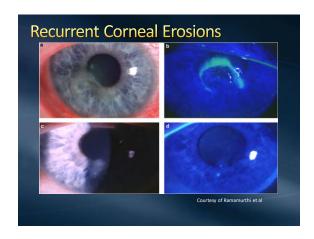
Indications Acute Chemical Burns Recurrent Corneal Erosions Neurotrophic Defects / Persistent Corneal Epithelial Defects Filamentary Keratitis Vernal Keratoconjunctivitis Recalcitrant Dry Eye Microbial Keratitis Nodular Degeneration PRK Haze

Corneal NeovascularizationThermal Corneal Burns

Indications Acute Stevens-Johnson Syndrome/Toxic Epidermal Necrolysis Post-infectious Recalcitrant Corneal Inflammation (e.g. herpetic, vernal, and bacterial) In conjunction with: Superficial Keratectomy High-Risk Corneal Transplantation Corneal ulcers, descemetocele or perforations Scleral melts Limbal graft for partial or total limbal stem cell deficiency Oculoplastic procedures including lid, fornix, and socket reconstruction Glaucoma Surgery Conjunctivochalasis and conjunctival reconstruction Petrygium surgery Bullous keratopathy Band keratopathy







Recurrent Corneal Erosions

- Epithelial cells rest on the basement membrane -128nm
 - Lamina Lucida made of glycoprotein laminin
 - secreted by overlying epi
 - Lamina Densa Made of Type IV collagen secreted by overlying epi
 - Lamina Reticularis Made of fibronectin secreted by underlying stroma
- Normal adherence to BM maintained by "adhesion complexes":
 - Hemidesmosomes (arrowhead)Lamina lucida and densa

 - Anchoring fibrils (arrows)
 - Fibronectin
 - Type IV and VII Collagen



Recurrent Corneal Erosions

- Matrix metalloproteinase (MMP)
 - Name for group of enzymes that break down the structure of the extracellular matrix (collagenase)
 - Gelatinase
 - Composed of MMP-9 and MMP-2
 - Degrades collagen type IV and VII and Laminin
 - all major components of BM
- Elevated levels of MMP-9 and MMP-2 have been observed in tears of patients with RCE
- Increased MMP-9 and MMP-2 expression have been implicated in the pathogenesis of RCE's
 - upregulation may lead to BM degradation and poor epithelial basement membrane adhesion.
- Higher than required levels of MMP may dissolve old and newly forming BM

Controlled Studies on RCE

- Cochrane Database Syst Rev. 2012 Sep 12;9:CD001861. doi: 10.1002/14651858.CD001861.pub3. Interventions for recurrent corneal erosions. Watson SL, Lee MH, Barker NH. Save Sight Institute, Sydney, Australia. stephanie.watson@sydney.edu.au.
- Cochrane Database Syst Rev Interventions for recurrent corneal erosions. Cochrane Database of Systematic Reviews 2007, Issue 4. Watson SL, Barker NH. Art. No.: CD001861. DOI: 10.1002/14651858.CD001861.pub2.

Stepwise Approach

- Medical Management
- Bandage CL
- Epithelial debridement
- Autologous Serum
- Surgical Intervention

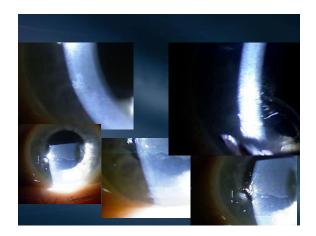
Stepwise Approach anagement Bar Epith erum Surgical Intervention

Combination Approach

- Best option is a combination Tx with a minimum of 4 individual tx options
- Trial and error to find the best combo for each
 - Epi debridement >>> Amniotic Membrane >>> >>> Autologous Serum >>>DCN
 - Epi Debridement >>> EW BSCL 12 weeks >>> DCN >>> Lotemax
 - ASP >>> BSCL 12 weeks >>> DCN >>> Lotemax

- 45 year old white male— Marathon runner
- October 2012: First visit seen on emergent basis
 - Scratched OD by his Dog
 - 2 linear abrasions detected
 - Healed as expected, Educated on possibility of RCE
- February 2013: RCE but reports minor events on and off for last couple of months
 - EW BSCL
- April 2013: RCE and on and off for weeks
 - EW BSCL and DCN
- Oct 2013: RCE
 - EW BSCL, DCN, Azasite, Muro





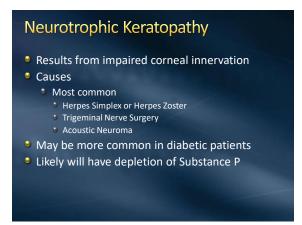


- Day 1 follow up
 Epithelium healing in
 Membrane fully intact
 Continue gatifloxacin QID, Pred Forte QID
 Day 3 follow up
 Epithelium almost completely healed
 Membrane dissolving. Open centrally
 Day 7 follow up
 Removed Prokera ring and placed an EW BSCL
 Continue Pred Forte QID for 1 week
 Continue gatifloxacin QD prophylactic
- Day 21
 Swapped out BSCL with another
 Continue Pred Forte BID for 5 weeks
 Continue gatifloxacin QD prophylactic
 Day 35, 49, 63, 77, 91
 Swapped out BSCL with another q2weeks
 Continue Pred until 8 weeks
 Been symptom free and no recurrences since December 2013

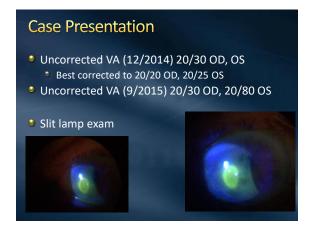


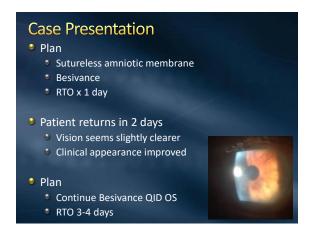
Persistent Corneal Epithelial Defects / Neurotrophic Defects • An epithelial defect is defined as persistent when it has failed to heal within a 2 week period. • (PED) occur when there is a failure of the mechanisms promoting corneal epithelialization. • results in disassembly of hemidesmosomes accompanied by degradation of Bowman's layer and stroma

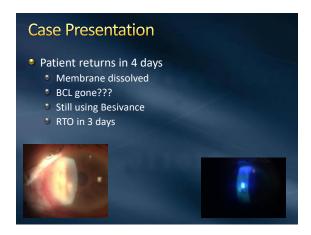
Persistent Corneal Epithelial Defects / Neurotrophic Defects • PED commonly occur in patients with: • Neurotrophic corneas • LSCD such as chemical injury • immune-mediated ocular surface disorders including atopic keratoconjunctivitis • ocular mucus membrane pemphigoid • Stevens-Johnson Syndrome • Peripheral ulcerative sclerokeratitis

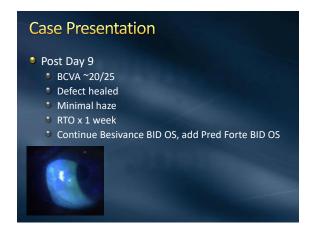


Case Presentation RM, 81 year old Caucasian male Presents with c/o blurred vision OS x 1 month Medical History Type II Diabetes Hyperlipidemia, hypertension Chronic kidney failure Ocular history Cataract surgery 10+ years ago Surgical history Tonsillectomy Trigeminal nerve surgery for cluster headaches



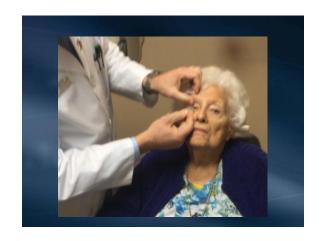










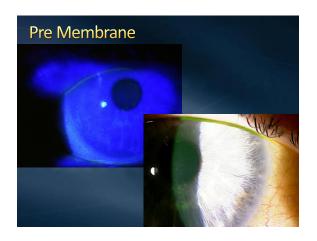




KeratoConjunctivitis Sicca

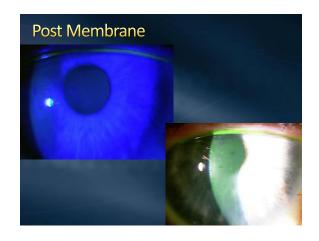
- Clinical findings
 - Tear film instability
 - Ocular inflammation
 - Pro-inflammatory cytokines are upregulated
 - Elevated levels of MMP noted
- Sutureless amniotic membranes contain antiinflammatory mediators, growth factors and cytokines
 - Help restore a healthy and non-inflamed ocular surface
 - Maintain a stable tear film

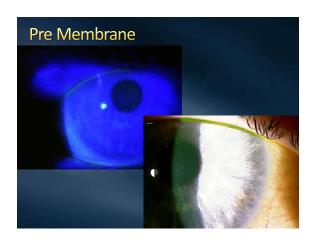
- Dryness is inflammatory condition
 AM is potent anti-inflammatory
 Great induction therapy that takes the place of corticosteroid to be used in addition to other therapies
 Restasis
 Autologous Serum
 DCN
- 64yo Caucasian female
 Initially Referred in for Sjögren's syndrome dry eye, previously tried everything under the sun
 Rated dryness irritation 9/10
 Would like to try something different that gives long lasting relief







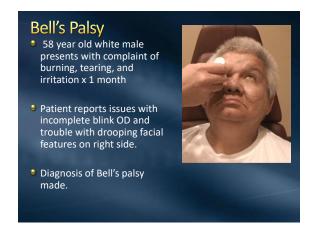




Dry Eye is a bilateral condition
 Typically space the placement 1-2 weeks apart from one another on Fridays
 Pt will be blurry regardless on which membrane used, so monocular approach is preferred
 Additionally prescribed Autologous Serum 4-6x / day
 Dehydrated membrane will dissolve in 2-3 days, cryopreserved 5-7, so typically will have lens / ring removed at that time



CN VII / Facial Nerve Palsy Can compromise the cornea in the setting of inadequate blinking and malpositioning of the midface and eyelid Facial nerve palsy can arise from a multitude of causes, although most cases are idiopathic Viral? A variety of non-surgical treatment modalities, ranging from scleral contact lenses to systemic steroids, have been explored and described in the literature





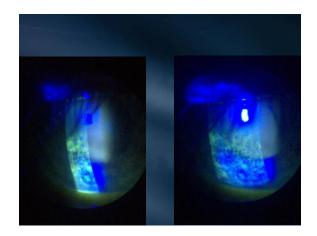


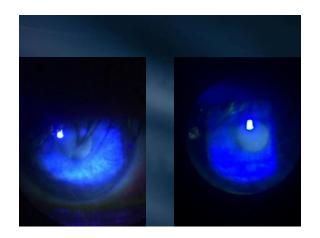


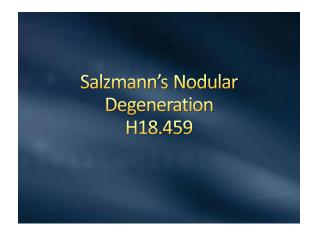
Going home instructions Vigamox BID OD Alrex ophthalmic suspension BID OD Due to incomplete blink, patient was asked to use a small piece of tape to create partial temporary tarsorrhaphy to hold AM and BCL in place. Patient instructed to return in 2-3 days



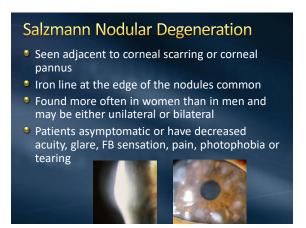








Salzmann Nodular Degeneration Slowly progressive degenerative process Idiopathic or in association with practically any significant corneal inflammatory disease Lesions appear as yellowish-white to blue elevated nodular lesions Single or multiple lesions Often annular in location and in the mid periphery



Salzmann Nodular Degeneration

- Exact cause still undetermined
 - Associated with previous inflammation of ocular surface
 - Keratitis
 - Dry eye
 - Pterygium
 - Long term CL wear
 - Stone et al demonstrated increased expression of MMP-2
- Large majority of patients have MGD, DES, previous CL wear
 - suggesting chronic ocular surface inflammation is part of the cause
 - Tx consists at targeted med therapy

66 yo WF Tx long term for Salzmann
 C/O FB sensation and pain, unbearable photophobia at times
 Manifest

 OD +4.25 -5.25 x 119 Add: +2.50 20/30 J2
 OS +2.50 -2.25 x 073 Add: +2.50 20/30 J1

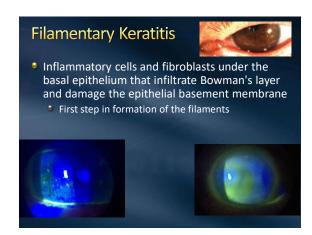
 Tx with Artificial tears, punctal plugs, Restasis BID OU and on and off Pred Forte for 5+ years
 Looking for a steroid sparing agent
 Plan was dehydrated membrane OD followed by

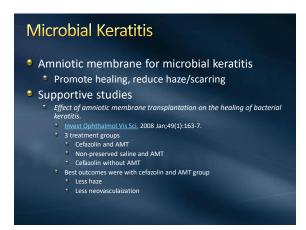
OS 1 week apart from one another

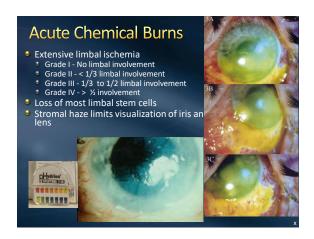
Ramp up steroid in anticipation











Acute Chemical Burns

- Two waves of intense inflammation
- First Wave occurs 12-24 hours after chem injury with infiltration of peripheral cornea with PMN and mononuclear leukocytes.
- Resulting from:
 - Blood elements from injured vessels in conj and uvea
 - Necrotic tissue of bulbar and tarsal conj
 - Chemotactically attracted byproducts of epi and stromal tissue
- Second, more aggressive wave of inflammatory cell infiltration begins at 7 days and peaks when corneal repair and degradation are maximal (bet 14-21 day)

Acute Chemical Burn

- Medical Management
 - Amniotic Membrane by day 3
 - Topical Pred Forte Q1h or Durezol Q2h x 7 d then taper & switch to
 - 1% topical medroxyprogesterone QID
 - 1% Atropine QD
 - Zymaxid / Moxeza / Besivance QID
 - Non Preserved artificial tears q1h
 - 100mg Doxycycline BID PO
 - 500 mg Diamox BID PO
 - Ultram 100mg PO q4-6h
 - Topical 10% ascorbate and 10% Citrate Q2h

Future Consideration

- Biologic Therapies are continuing to expand
 - Over 900 studies being performed for Biologic therapies
 - Anticipate increased utilization over next 5 years
 - Amniotic Gel / Ointment
 - Amniotic Drops

Conclusion

- Use of sutureless amniotic membranes has shown to provide valuable tool to control inflammation and promote epithelialization
- Indications for use are increasing and recommending considering its usage earlier in the treatment paradigm

Conclusion

- Recommendations
 - Promote Epithelialization
 - Suppress Inflammation
 - Inhibit Scarring
 - Practice makes perfect
 - Don't wait for last resort treatment
 - Did wetlab/hands on workshop this morning
 - Thanks to our wetlab donors



