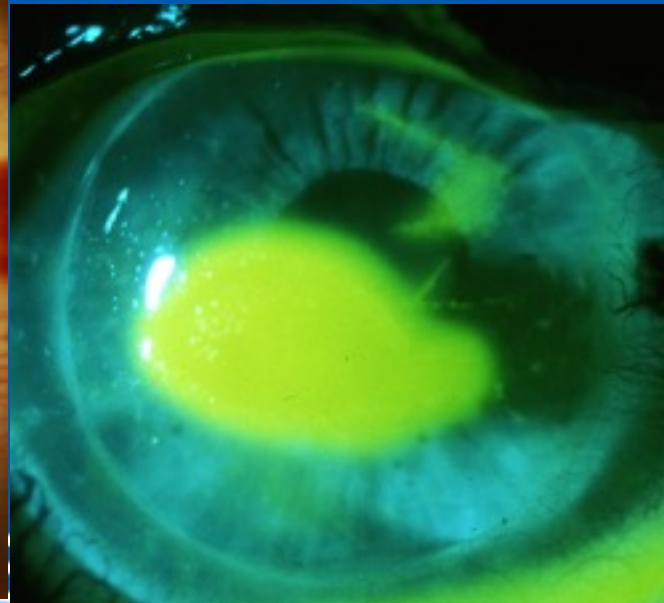
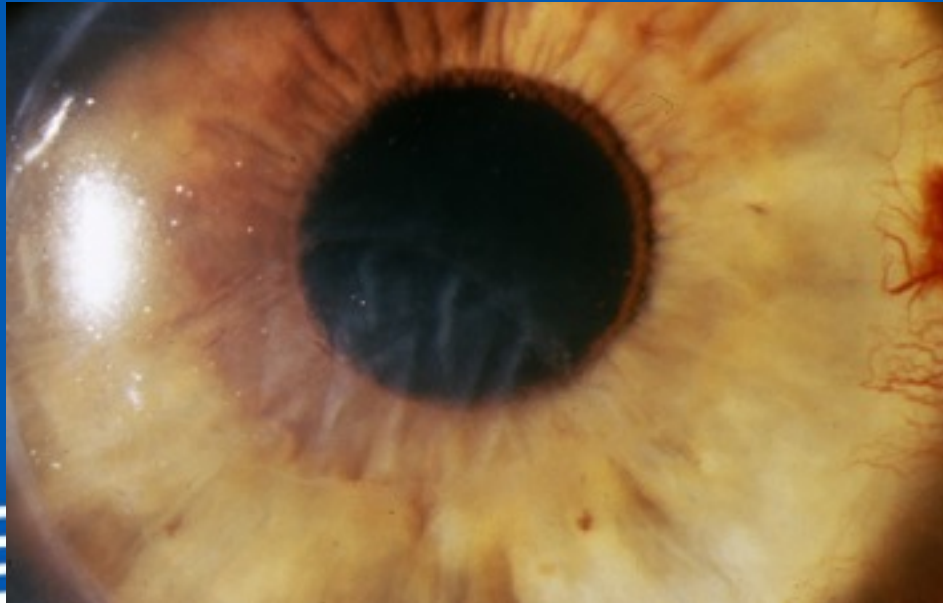


Corneal Erosions and Persistent Epithelial defects, Will they ever heal?

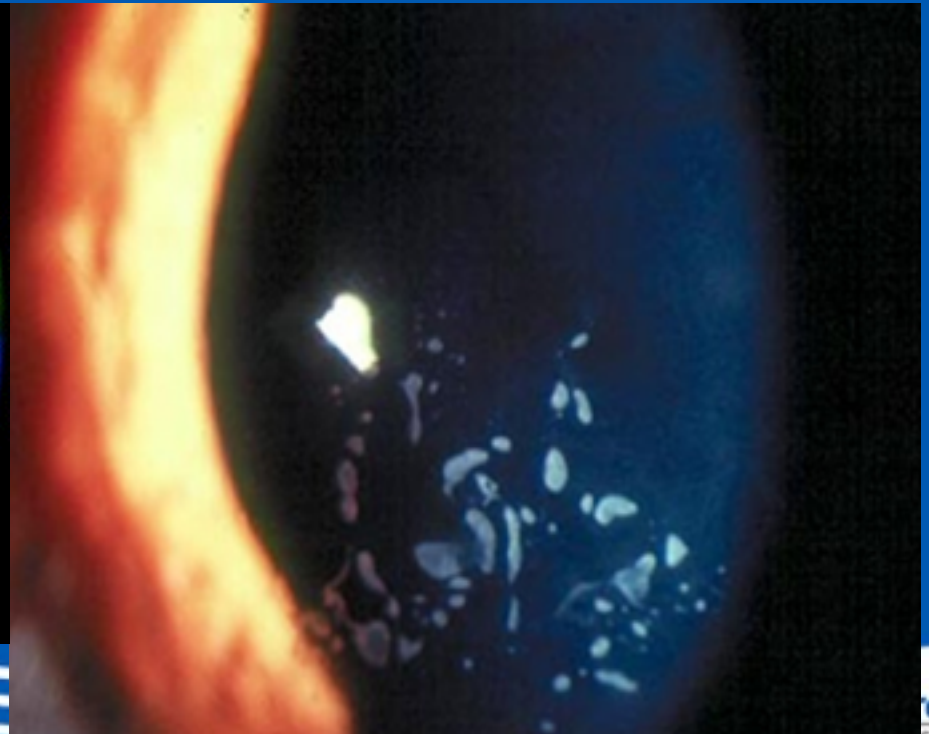
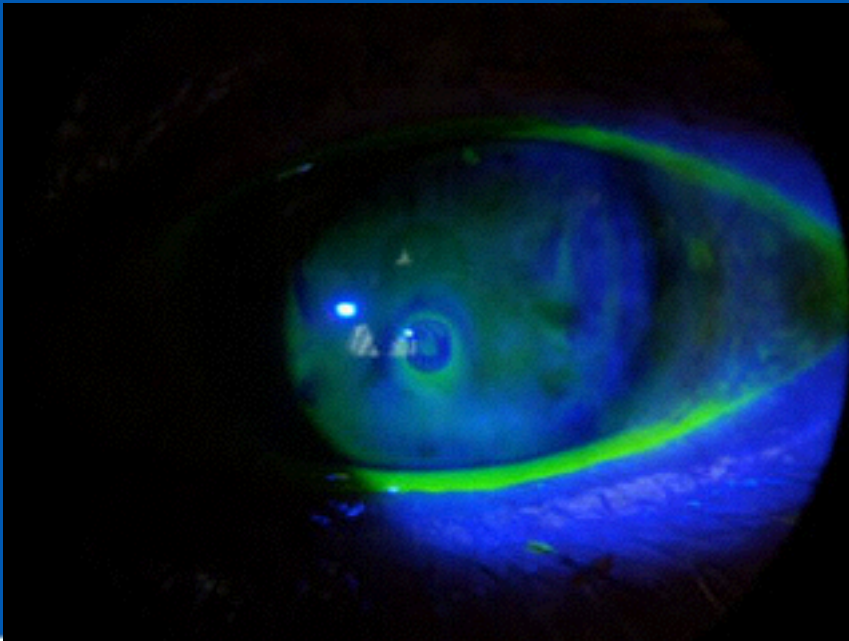
Marian S Macsai, MD
Professor of Ophthalmology
University of Chicago Pritzker School of Medicine
Chief of Ophthalmology
NorthShore University HealthSystems



I have no proprietary or financial interest in any of the products discussed.

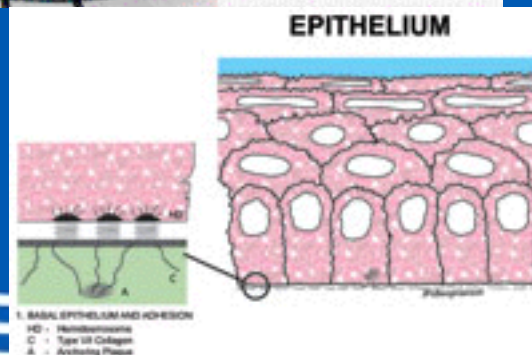
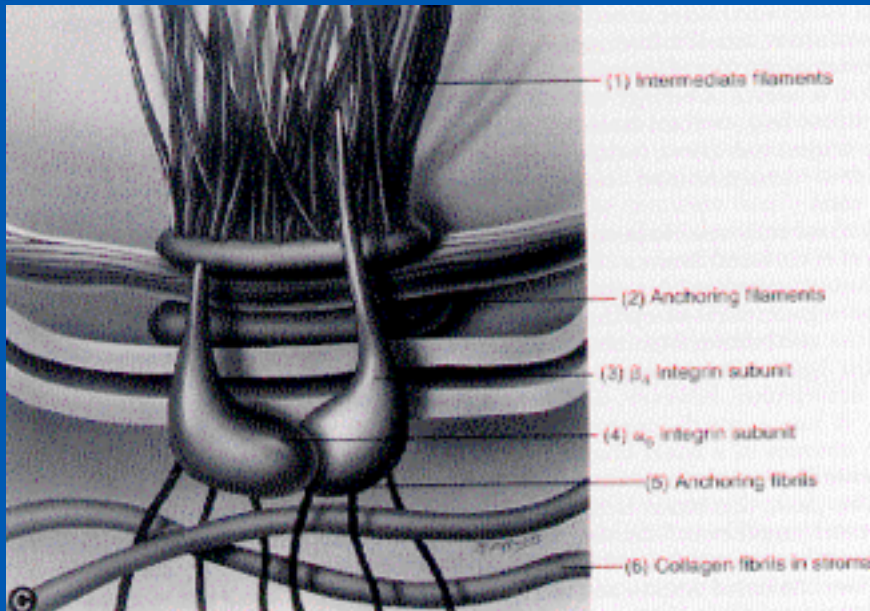
Recurrent Corneal Erosions

- Epithelial Basement Membrane
- Defective Adhesions; hemi-desmosomes
- Recurrent breakdowns of the epithelium



Basement Membrane Zone

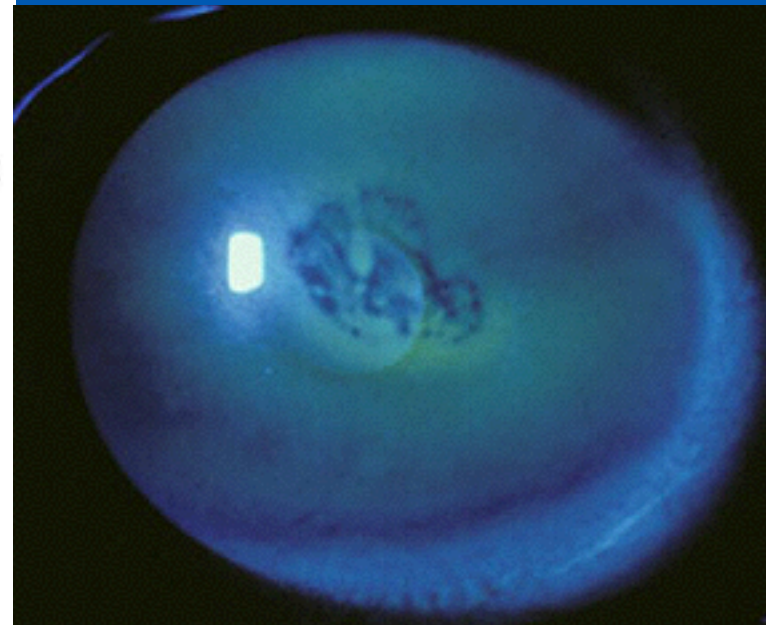
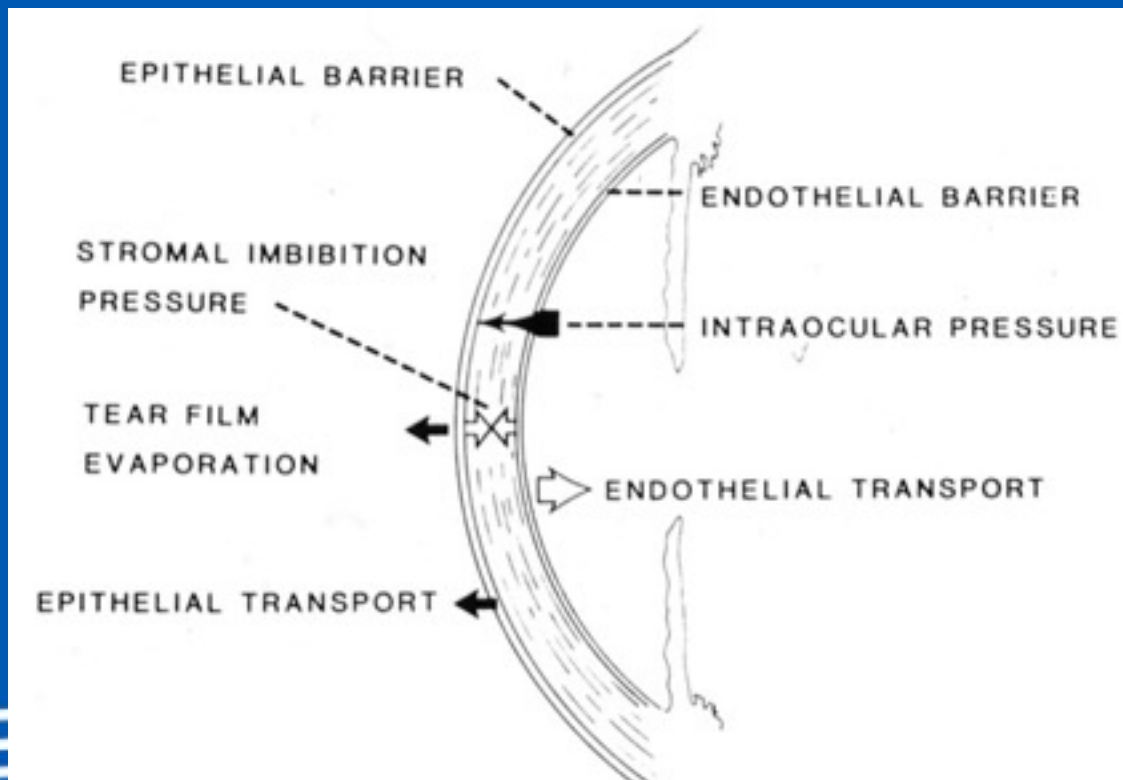
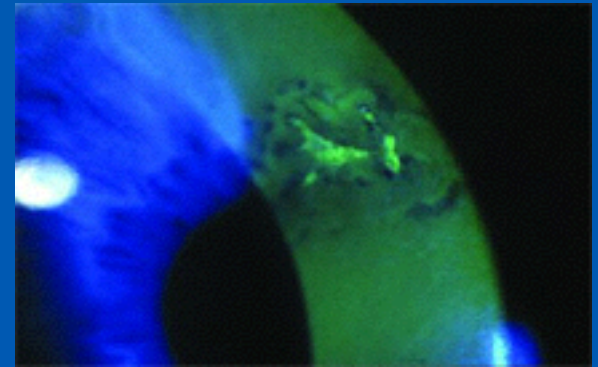
- Complex adhesion between basal cells and ant stroma



LEIDOWITZ, 1998

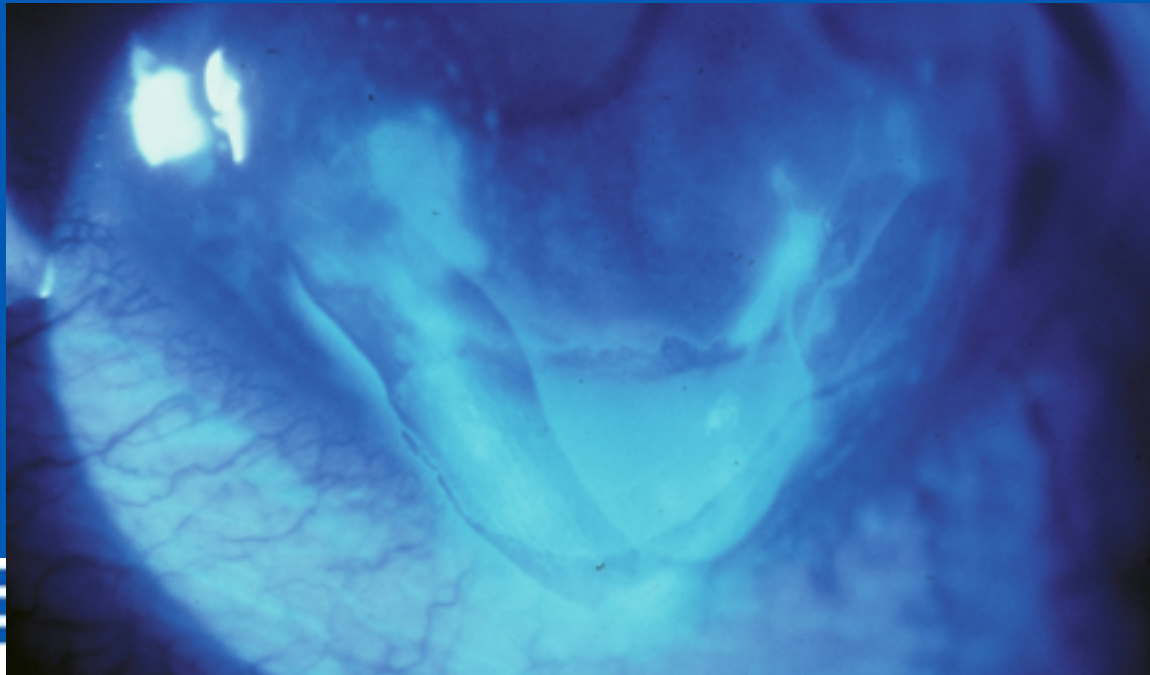
Recurrent Corneal Erosions : What Happens?

- Cornea swells during sleep
- Tear Production decreases



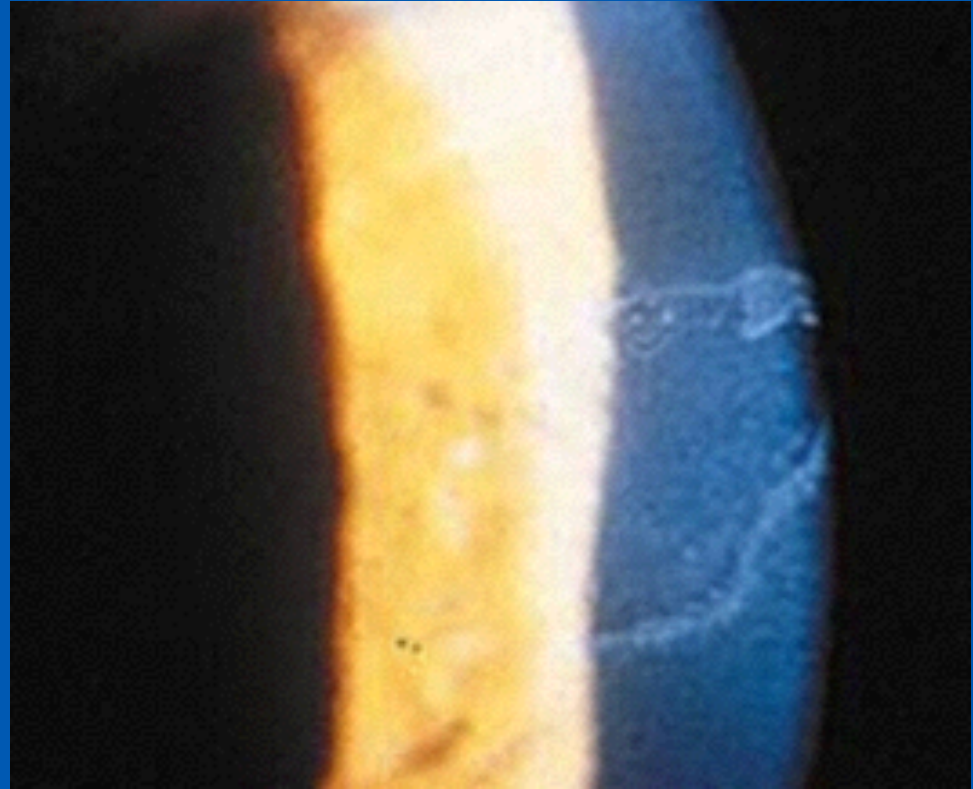
Recurrent Corneal Erosions : What happens?

- Faulty basement membrane adherence.
- Basal epithelial cells fail to produce proper basement membrane complexes to attach to the Bowman layer or hemi-desmosomes



RCE types

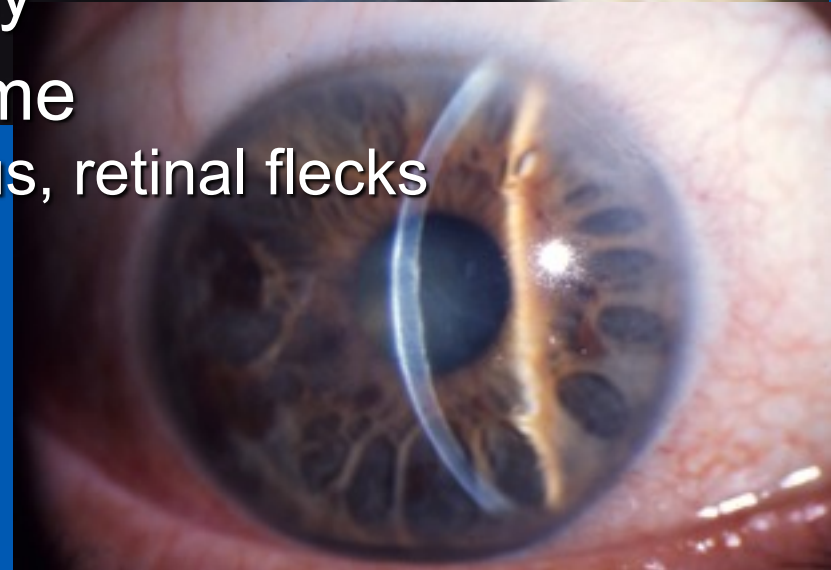
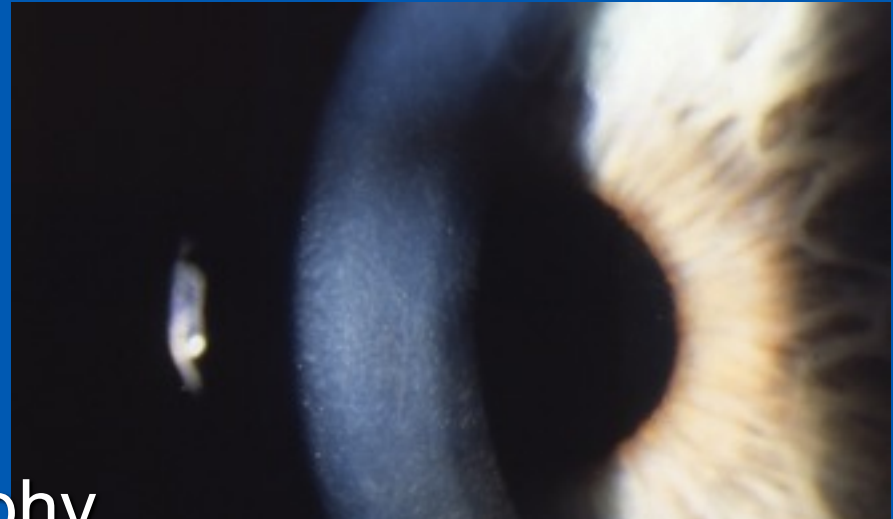
- Spontaneous
- Traumatic
- Secondary
 - Diabetes
 - Corneal Dystrophy

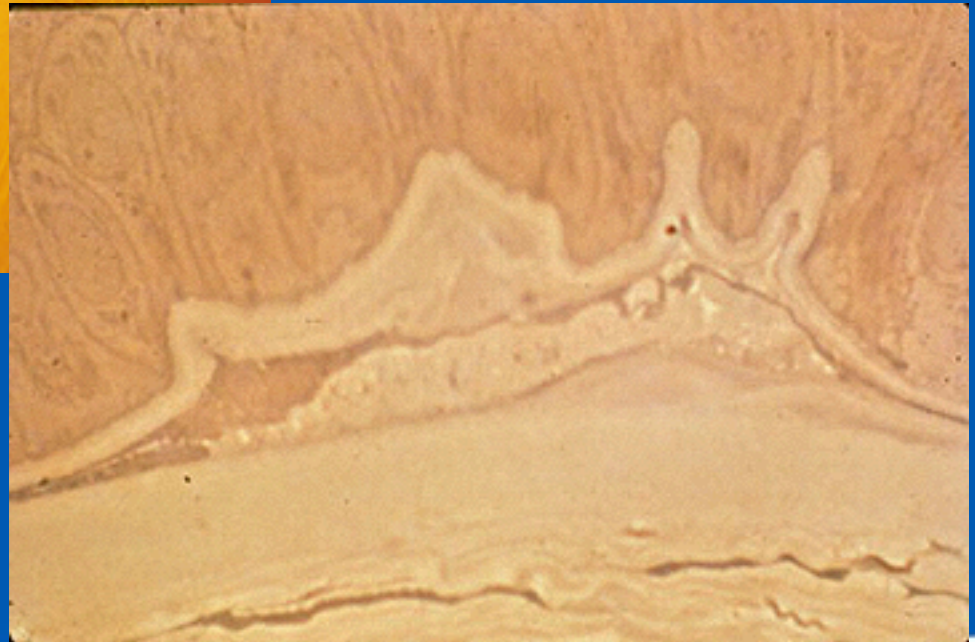
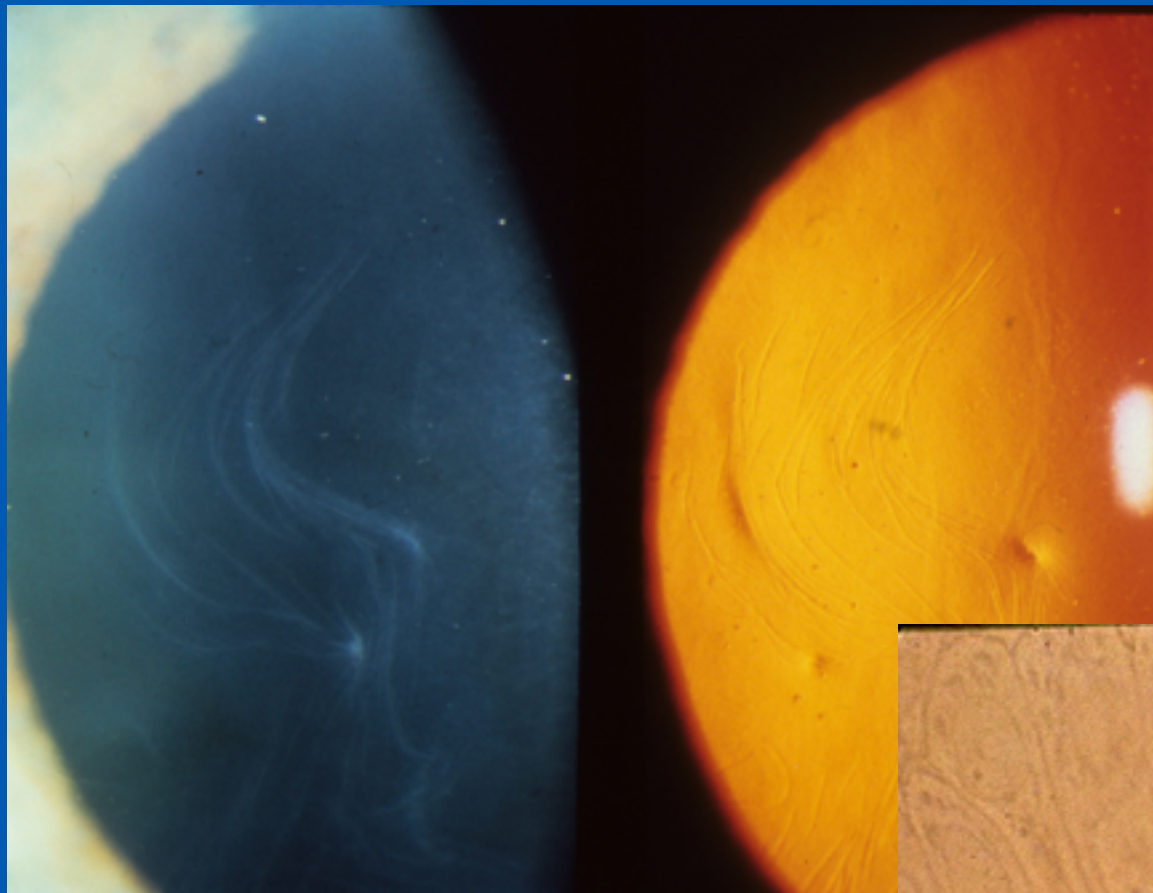


Laibson PR. Epithelial basement membrane dystrophy and recurrent erosions.
In: *Current Ocular Therapy*. 5th ed. 2000:355-357.

Dystrophy

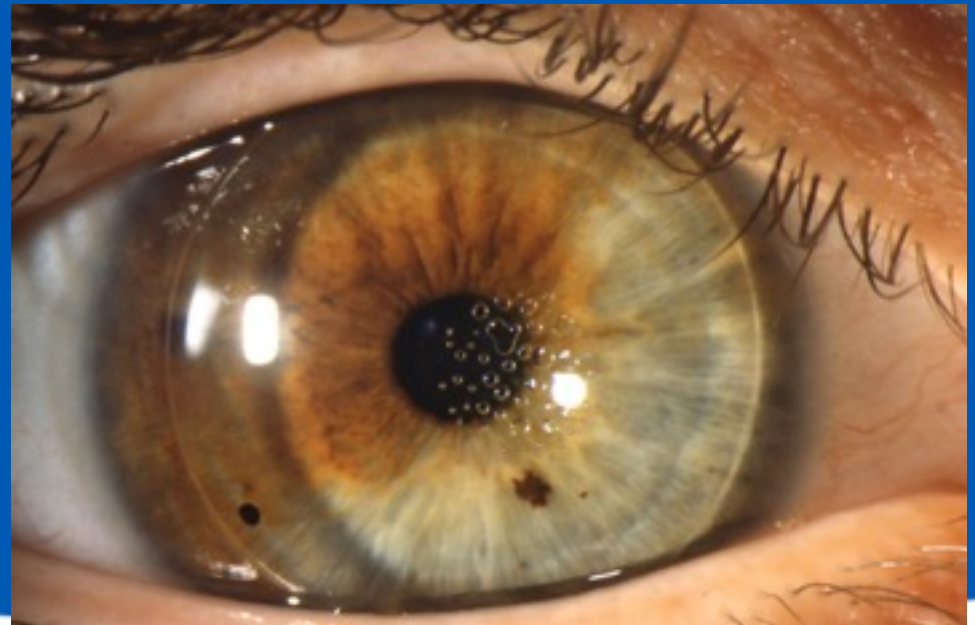
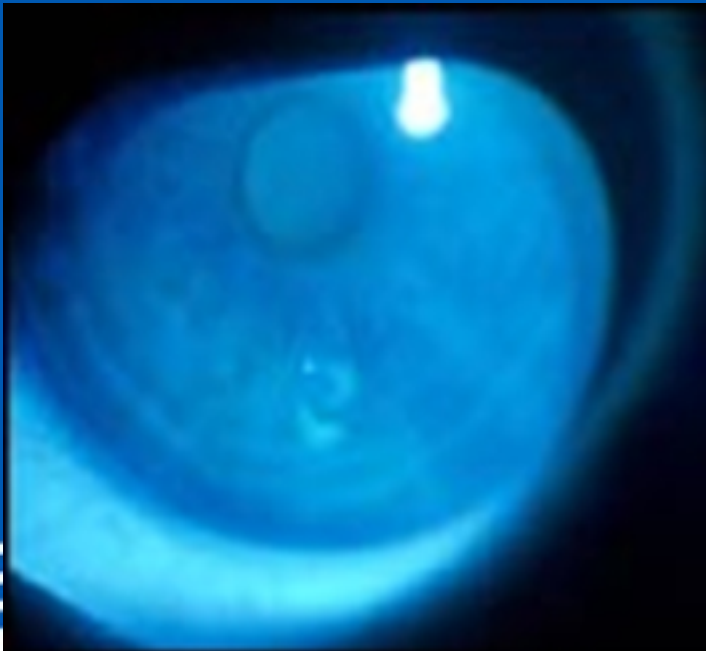
- EBMD
 - Bilateral, asymmetric
- Fuchs Bilateral guttata
- Reis-Bucklers
- Lattice Corneal Dystrophy
- Juvenile Alports Syndrome
 - x-linked, anterior lenticonus, retinal flecks





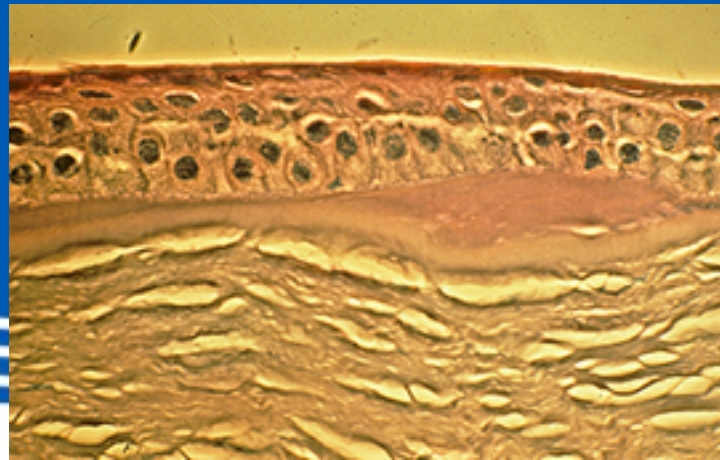
Trauma

- Superficial Abrasion
 - no disruption of bowmans layer
- Deep
 - Penetration or disruption of Bowmans
- Fingernails, FB, Contact lenses, Chemicals, brushes, branches



Electron Microscopy

- Separation of the anchoring system at the level of the epithelial cell membrane
- Normal and degenerate PMNs found within and between the epithelial cells and the anchoring layer.
- Degenerate PMNs may secrete metalloproteinases that cleave the Bowman layer below the anchoring system.



Findings

- Preceding trauma, 3-10 days
- Epithelial Microcysts
- Surface irregularity, negative stain, dendritiform
- Multiple recurrences



Moutray TN, Frazer DG, Jackson AJ. Recurrent erosion syndrome--the patient's perspective. *Cont Lens Anterior Eye*. Jun 2011;34(3):139-43.

Differential Diagnosis Clinical Exam

- Foreign Body
- Dry Eyes
- Corneal Dystrophy
- Floppy lid
- Contact Lens Complications

Reeves SW, Kang PC, Zlogar DF, Gupta PK, Stinnett S, Afshari NA. Recurrent Corneal Erosion Syndrome: A Study of 364 Episodes. *Ophthalmic Surg Lasers Imaging*. Mar 9 2010;1-2.

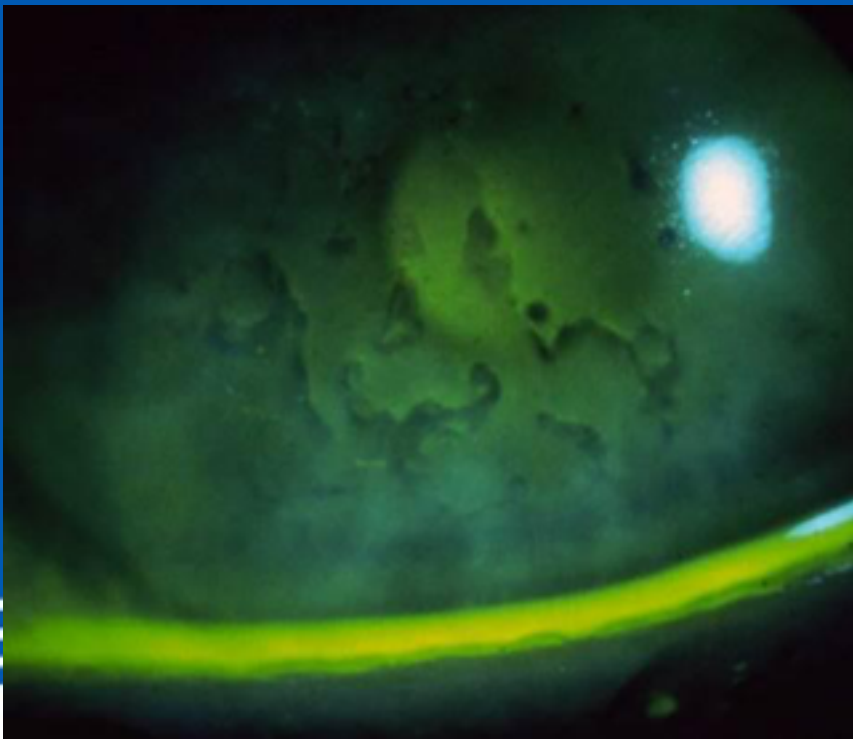
Work up

- Flip the lid to look for foreign body-floppy lid
- Suspect dry eye, be liberal with plug in lower puncta
- Look for EBMD
- Contact lens fit? Tear?



Findings

- Corneal Edema-negative stain
- Topography –focal areas of corneal flattening, corneal lagoons
- Wet Q tips, areas of loose adhesions



Medical Tx

- Regenerate Epithelium and restore adhesions (8- 12 weeks)
- SPP/AB/HAT
- Punctal occlusion,
- Hypertonic Saline Ointment 5%
- Debridement of the epithelium and diseased Basement Membrane
- Bandage Contact Lens (8-26 weeks), plug
- Anterior Stromal Puncture

Fraunfelder FW, Cabezas M. Treatment of recurrent corneal erosion by extended-wear bandage contact lens. *Cornea*. Feb 2011;30(2):164-6

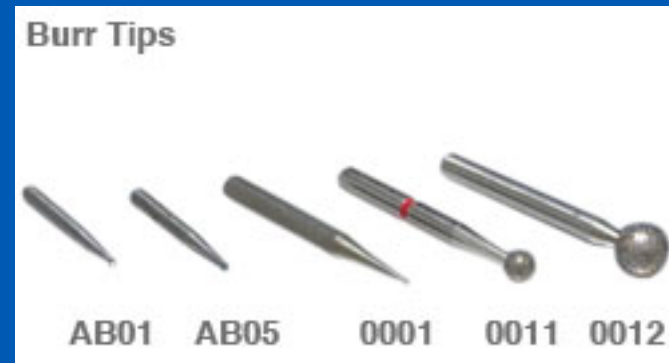
Risk of Recurrence

- Hykin et al
- 117 patients, 38 yrs old, 6-16 mo fu
- Highest risk in Trauma and EBMD, lower ½ cornea
- 5 % not resolved after 5 days with SPP/OINT/
CYCLO
- 5% failed prophylactic ointment

Hykin PG, Foss AE, Pavesio C, Dart JK. The natural history and management of recurrent corneal erosion: a prospective randomised trial. *Eye*. 1994;8 (Pt 1):35-40

Treatment

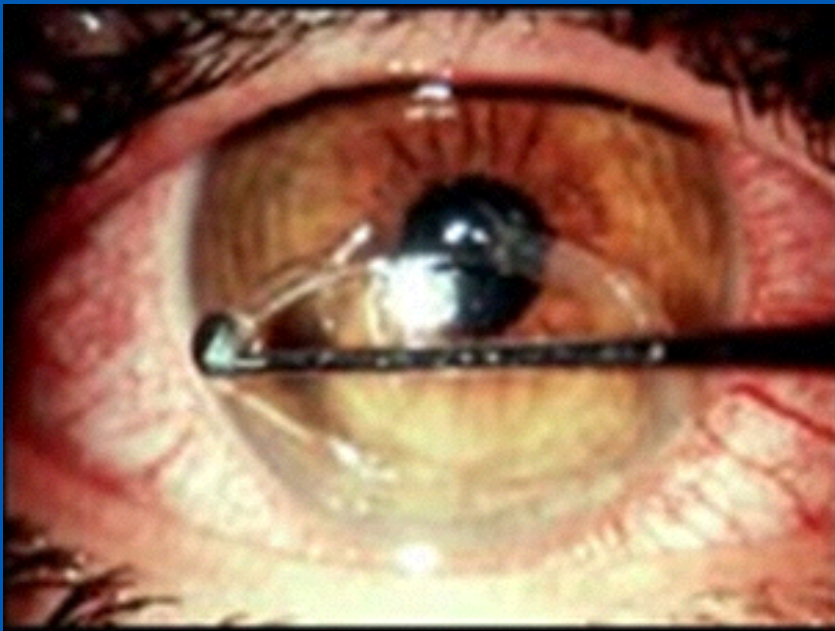
- Mechanical debridement
- Diamond Burr
- Delamination of corneal epithelium
- 20% alcohol soln applied to cornea for 30-40 seconds, epithelium removed, irrigate with saline, BCL placed



Mencucci R, Paladini I, Brahim B, Menchini U, Dua HS, Romagnoli P. Alcohol delamination in the treatment of recurrent corneal erosion: an electron microscopic study. *Br J Ophthalmol.* Jul 2010;94(7):933-9.

Debridement

- Remove epithelium and smooth Bowmans at the slit lamp
- Not the foreign body diamond Burr

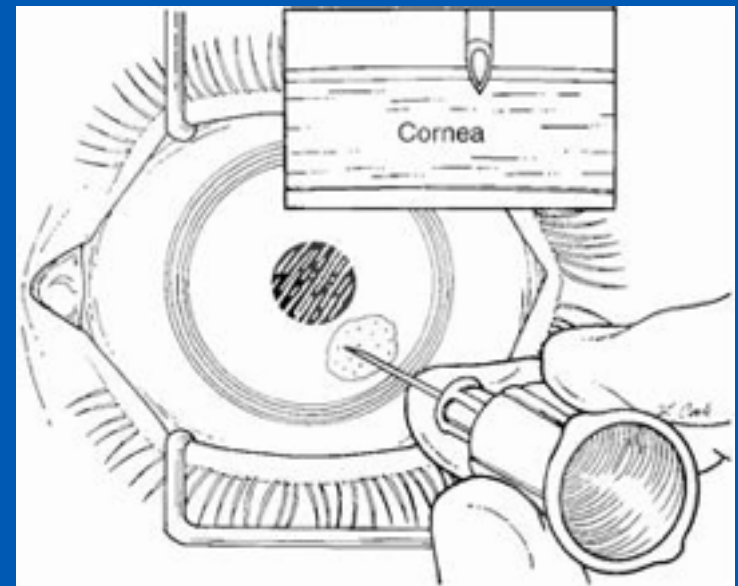


Anterior Stromal Puncture

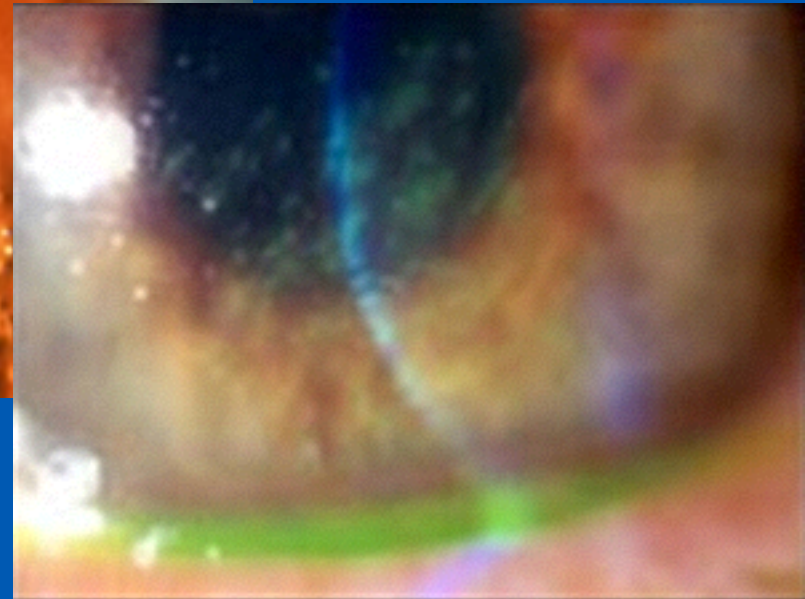
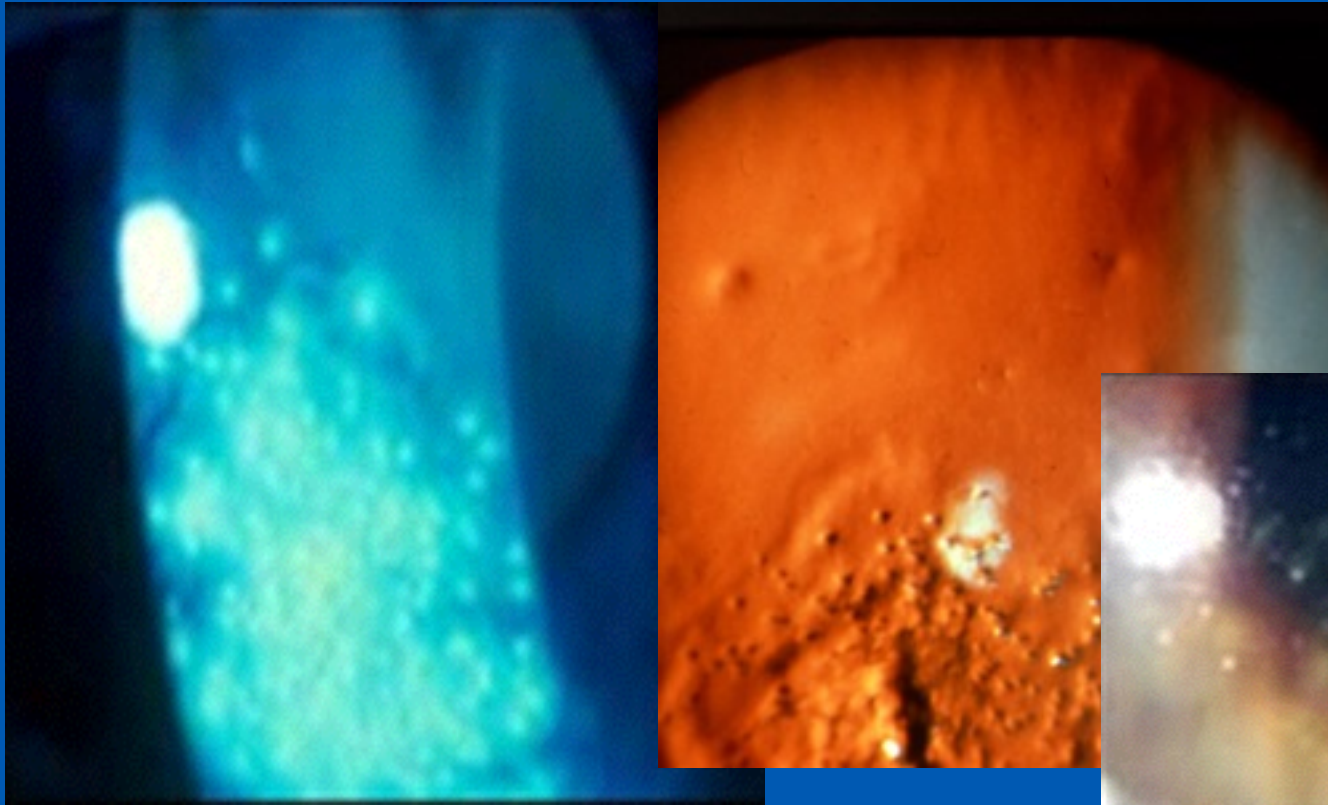
- Soft Tech, curved needle 0.1 mm thru epi
- ◉ 75-150 small punctures with a Rubinfeld needle through the epi and Bowmans into anterior stroma, through loosened epithelium or epi defect, making micropunctures to the anterior stroma.
- ◉ 90% response with one tx



Maréchal-Courtois C, Duchesne B. [Recurrent corneal erosion]. *Bull Soc Belge Ophthalmol.* 1993;247(1):13-5

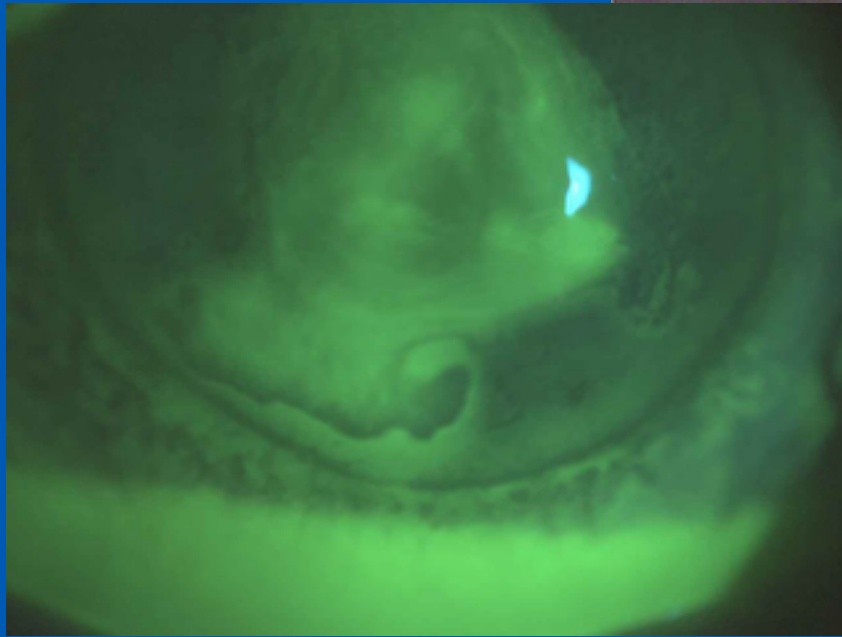
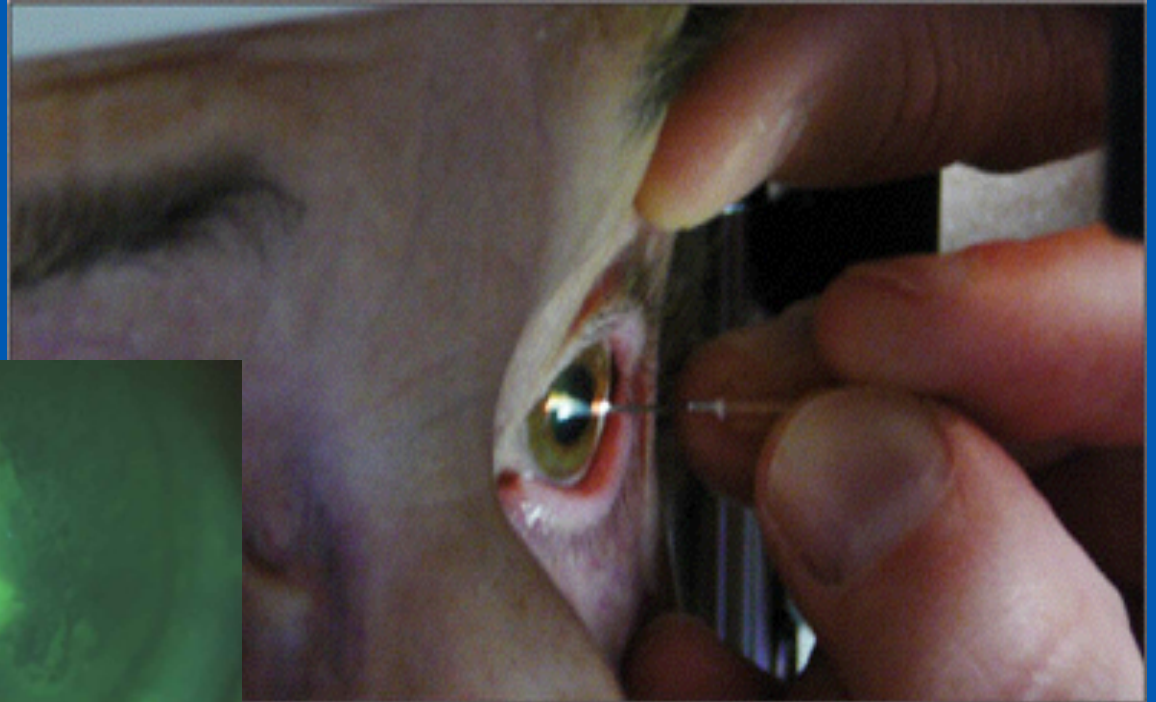


Anterior Stromal Puncture



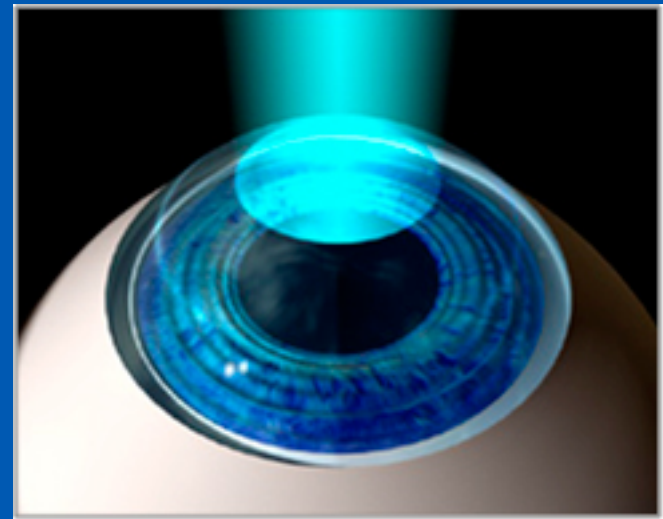
Maréchal-Courtois C, Duchesne B. [Recurrent corneal erosion].
Bull Soc Belge Ophtalmol. 1993;247(1):13-5

Anterior Stromal Puncture



PTK

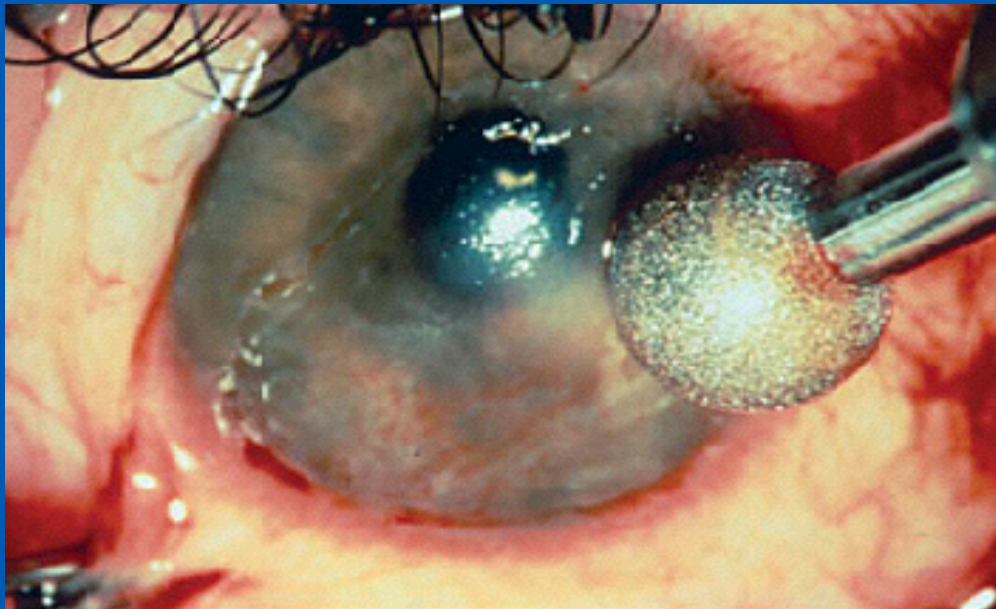
- Remove the epithelium and spot treatment over whole area of loose epithelium
- Use of a large spot size, such as 5 mm, apply 16 pulses
- 75-100% cure rate



John ME, Van der Karr MA, Noblitt RL, Boleyn KL. Excimer laser phototherapeutic keratectomy for treatment of recurrent corneal erosion. *J Cataract Refract Surg.* Mar 1994;20(2):179-81.

Diamond Burr

- Diamond Burr applied to bare Bowmans layer after epithelial debridement
- BCL, punctal plugs, cycloplegia



Soong HK, Farjo Q, Meyer RF, Sugar A. Diamond burr superficial keratectomy for recurrent corneal erosions. *Br J Ophthalmol.* Mar 2002;86(3):296-8.

Yag Laser Tx

- 0.4-0.5 mj pulses applied to Bowmans through intact epithelium



Katz HR, Snyder ME, Green WR, Kaplan HJ, Abrams DA. Nd:YAG laser photo-induced adhesion of the corneal epithelium. *Am J Ophthalmol.* Nov 15 1994;118(5):612-22.

Recurrent Cornea Erosions : Medical Tx

- Regenerate Epithelium and restore adhesions (8- 12 weeks)
- SPP/AB/HAT
- Punctal occlusion,
- Hypotonic Saline Ointment 5%
- Bandage Contact Lens (8-26 weeks)
- Debridement of the epithelium and diseased Basement Membrane
- Anterior Stromal Puncture

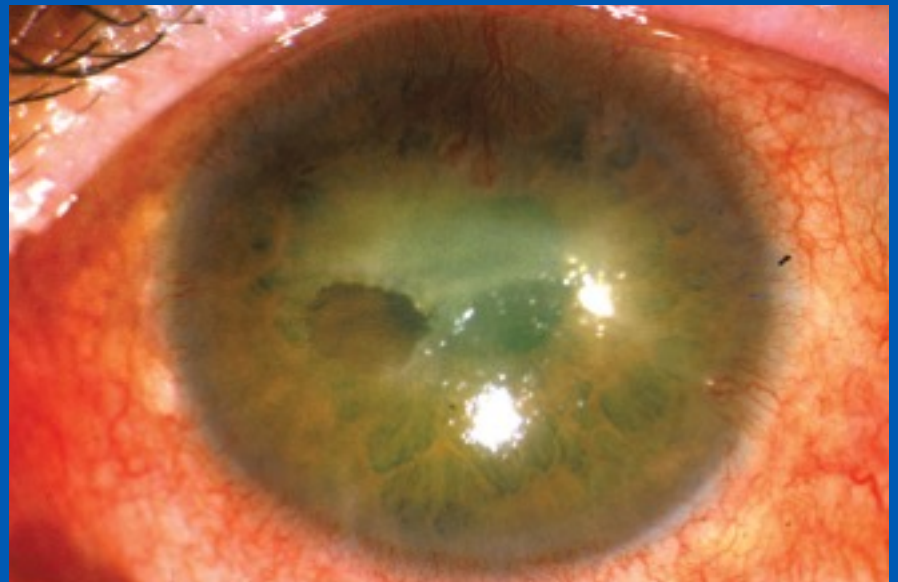
Fraunfelder FW, Cabezas M. Treatment of recurrent corneal erosion by extended-wear bandage contact lens. *Cornea*. Feb 2011;30(2):164-6

Recurrent Cornea Erosions : Surgical Treatment

- Anterior Stromal Puncture
 - Non visual axis
- Debridement
 - Painful
- Diamond Burr
 - Sub epithelial Scaring?
- Yag Laser Tx
 - No debridement
- PTK
 - Debridement and smoothing of Basement Membrane

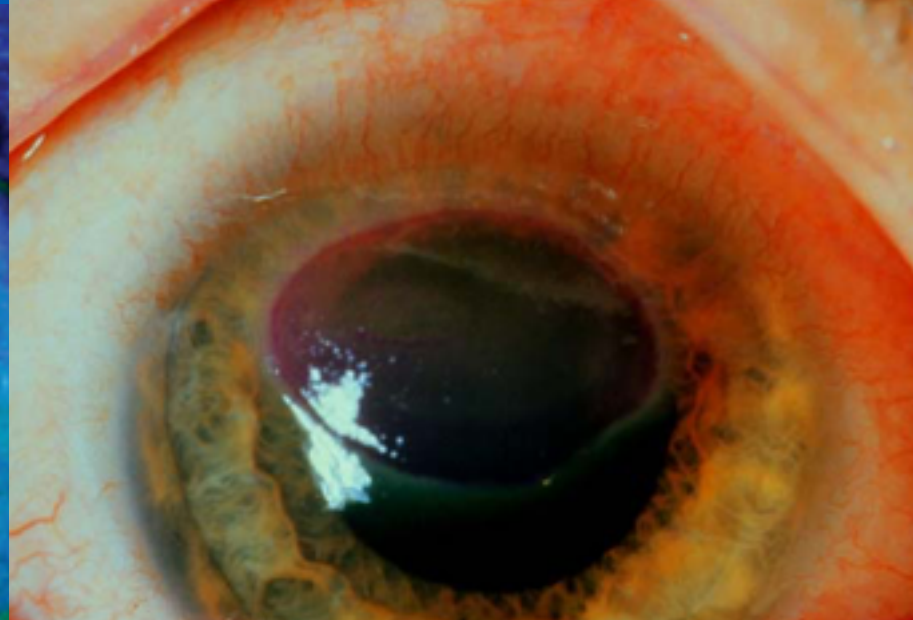
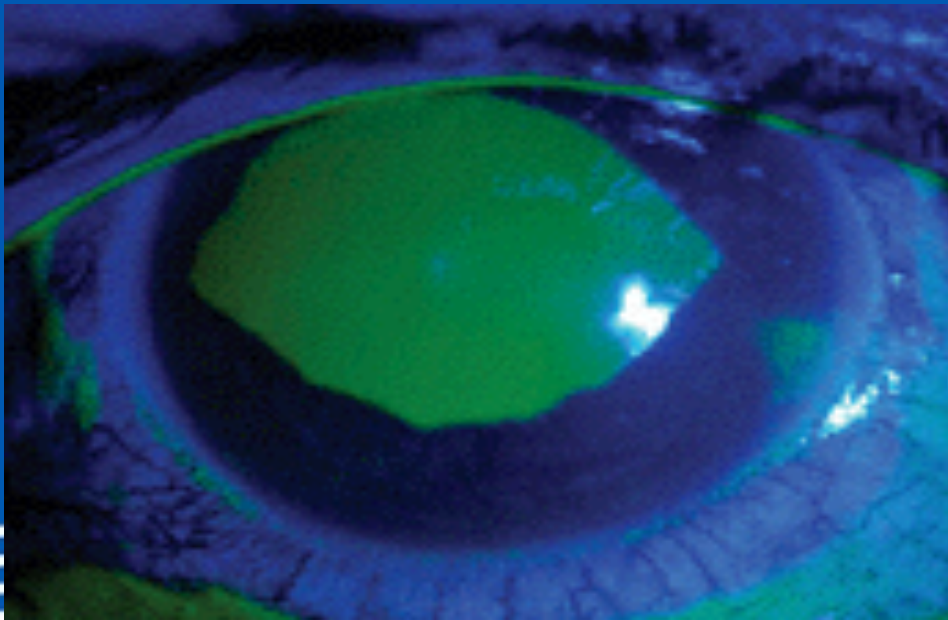
Persistent Epithelial Defects

- Definition
- Medication
- Lubrication
- Occlusion
- Growth Factors



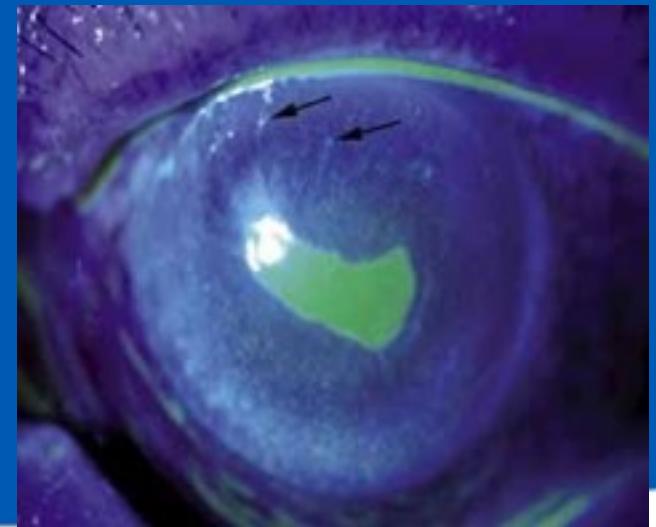
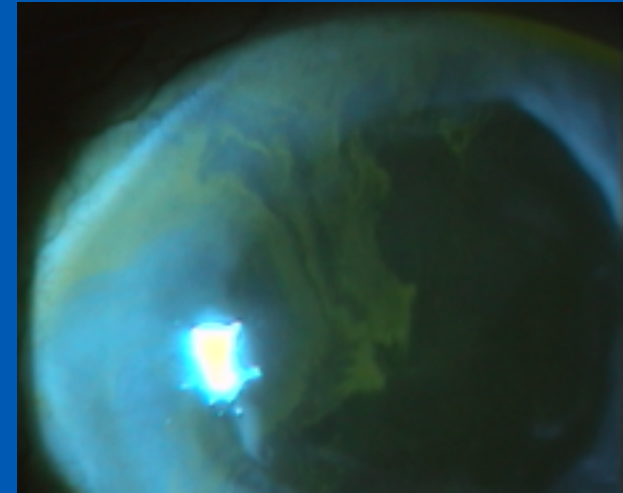
PED Definition

- Definition
 - “An epithelial defect that does not heal in the expected amount of time”
 - A defect that has been treated for two weeks without resolution



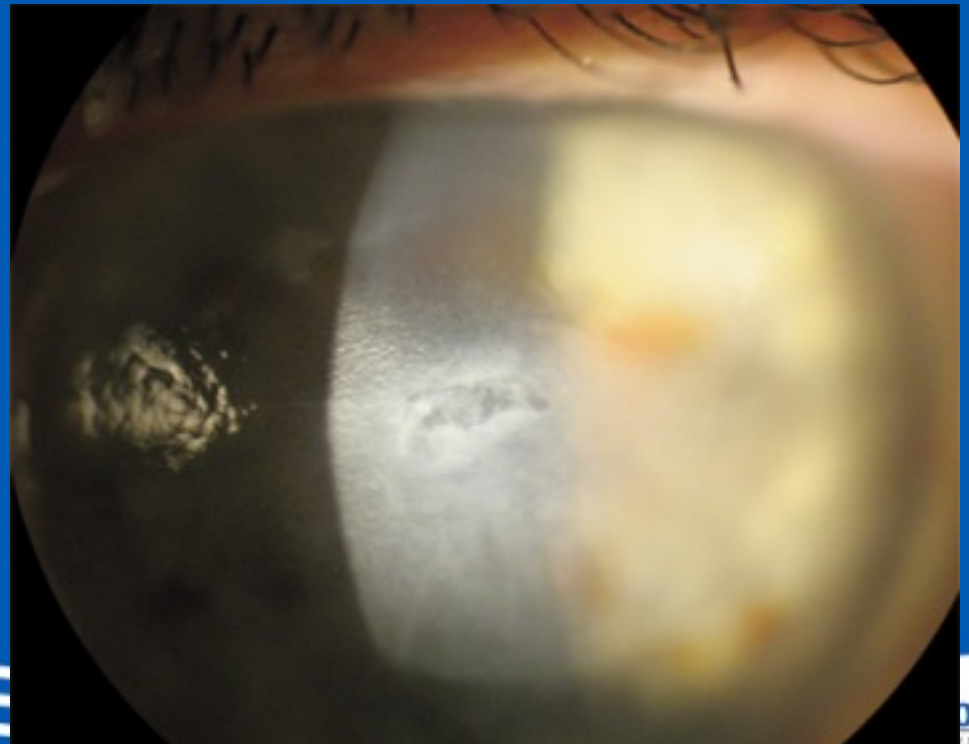
PED Risk Factors

- Corneal hypesthesia
- Diabetic Keratopathy
- Limbal stem Cell Deficiency
 - » Look for it with Late FI Staining
- Dry Eye Disease
- Exposure Keratopathy
- Neurotrophic Keratopathy
 - » Prior PK
 - » HERPES
 - » Diabetes..



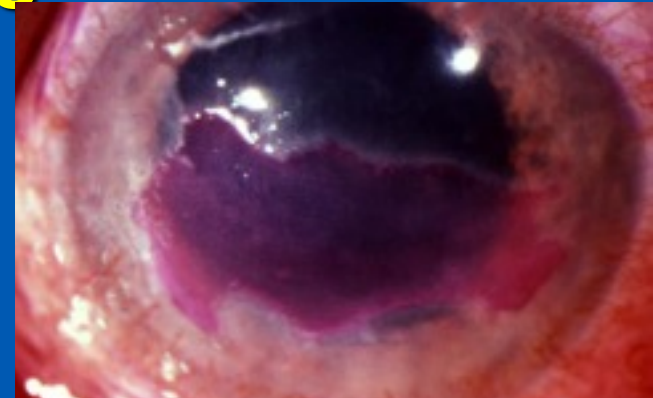
PED Potential Complications

- Loss of vision
 - Sub Epithelial scarring and Haze
- Infection
- Melting
- Perforation



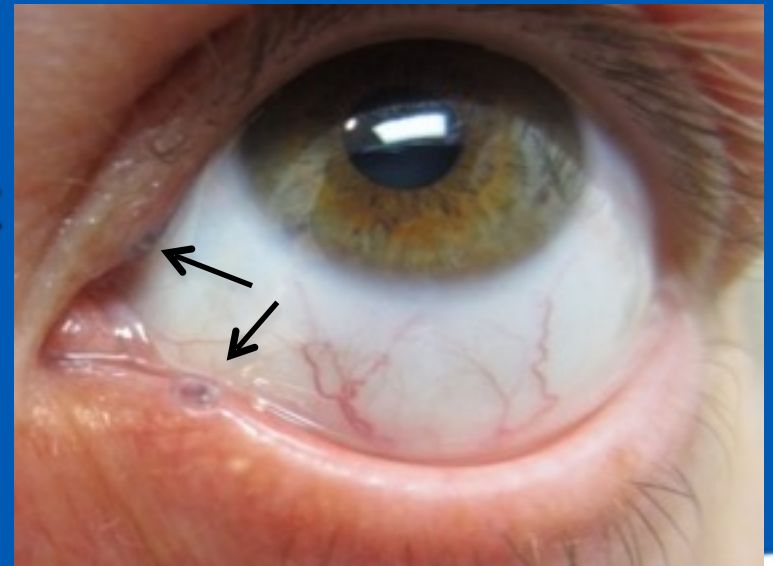
PED Medications

- Stop Drops – Medicamentosa
- Preservative Free Antibiotics
- Oral Diamox for iop management
- Atropine for cyclopegia
- Stop topical antiviral medications, use oral



PED Increase lubrication

- Preservative Free Artificial Tears
- Punctal occlusion (plugs, Cautery)
- Treat the underlying Dry Eye
- Omega 3 TG
- Cyclosporin
- DHEA drops
- Retinoic Acid ointment



[Cornea](#). 2013 Jun;32(6):761-5. Epithelial healing using omega-3 oral nutritional supplements before and after PRK. [Ong NH](#), et.al

PED- Occlusion

- Bandage Contact Lens
– 30-day
- Patch
- Botox
- Lid Splint

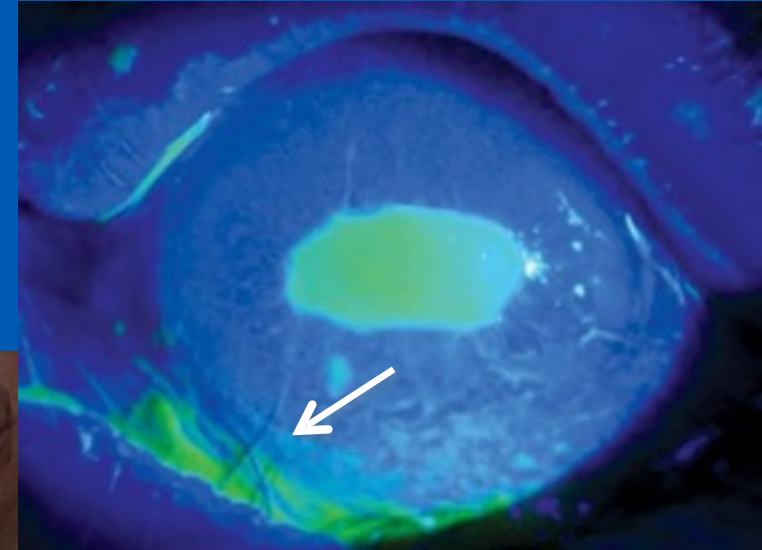


[Cornea](#). 2002 Apr;21(3):260-4.
The Stamler lid splint
[Arch Ophthalmol](#). 2006;124(4):546-549
Robinson, Tantri, Shriver, Oetting,



PED – Lid Malpositions

- Trichiasis
- Lagophthalmos
- Floppy Lids



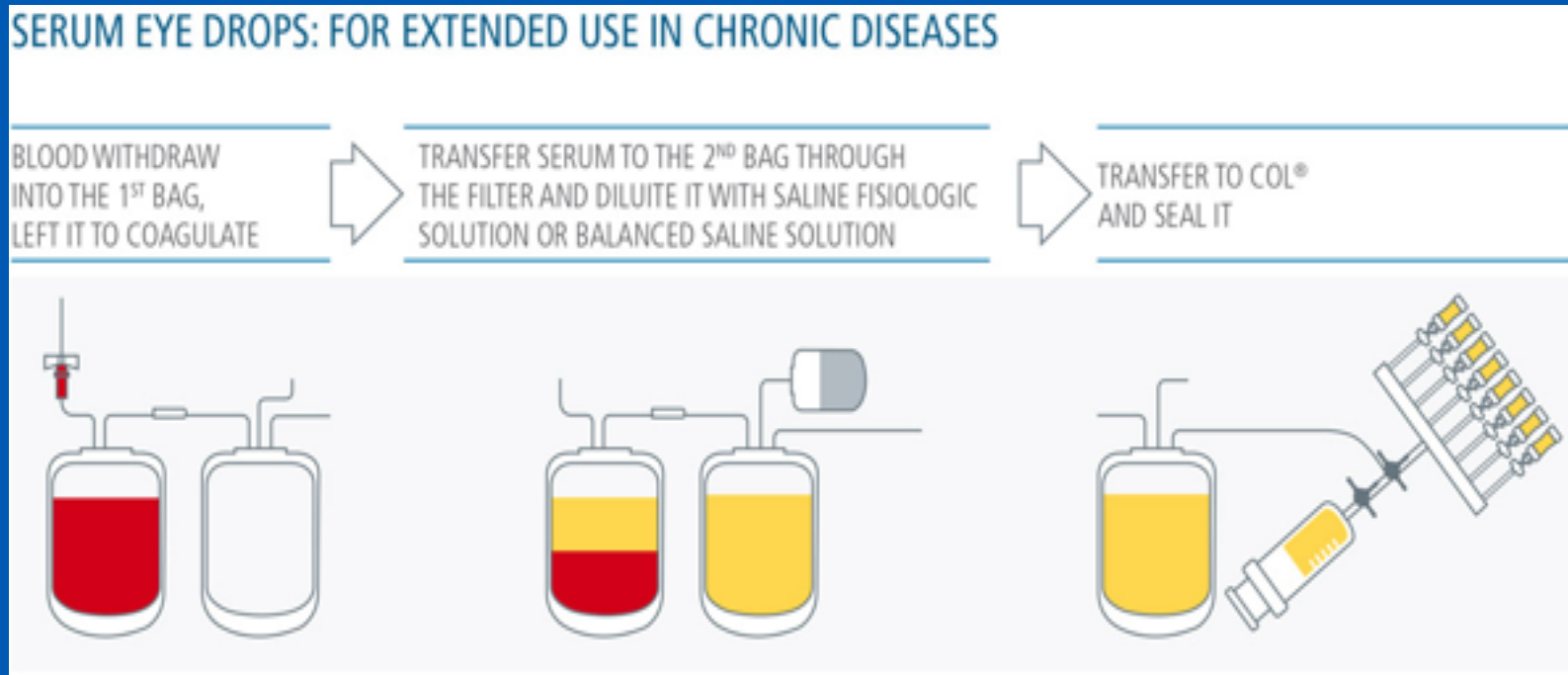
PED – Increase Growth Factors

- Autologous Serum 20-50%-(vitamin A, substance P, immunoglobulins, and fibronectin)
- Vitamin C (aid in collagen repair and stability)
- Doxycycline-prevent stromal lysis.(20-100 mg twice daily)
- Amniotic Membrane
- Nexagon
- Thymosin β 4
- Connexin 43
- Mesenchymal Stem Cells

Chang BH et al. Neurotrophic keratitis. In: Krachmer JH et al., eds. *Cornea*. Philadelphia: Elsevier 2011:1101-1108. Young AL et al. *Eye (Lond)*. 2004;18(6):609-614

PED – Autologous Serum

- 20-100% shown to increase the rate of healing in PED
- Ready Made ABO-Specific 20%



[Biomed Res Int. 2013;2013:5213-15](#), [Acta Ophthalmol. 2014 Dec;92\(8\):783-6](#), [Eye Contact Lens. 2015 May;41\(3\):133-40.](#)

PED- Amniotic Membrane

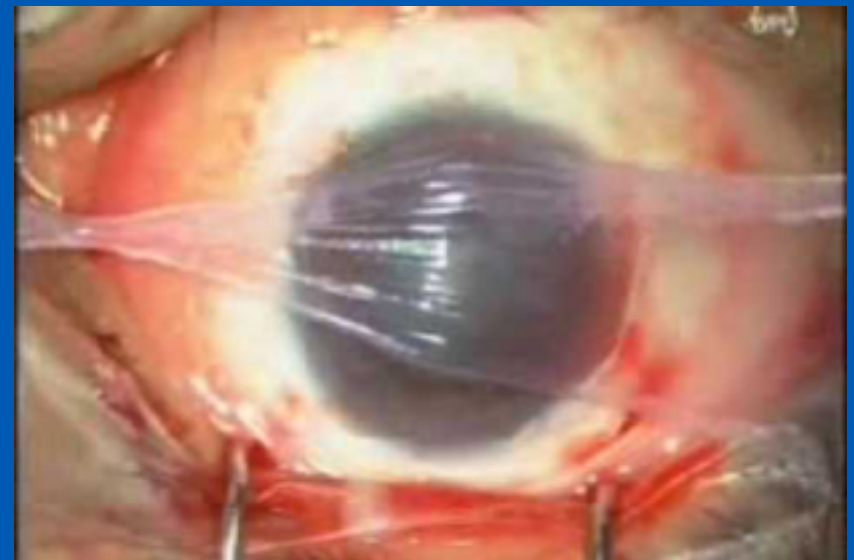
- Inner avascular layer of the 3- layered fetal membrane
- Substrate for epithelial cell migration and attachment
- Cytokines and growth factors including EGF and fibronectin
- Frozen (-80° C) or Freeze Dried
- Amniotic Extract recent efficacy
- Placed under a SCL

[Coll Antropol.](#) 2013 Apr;37 Suppl 1:161-4



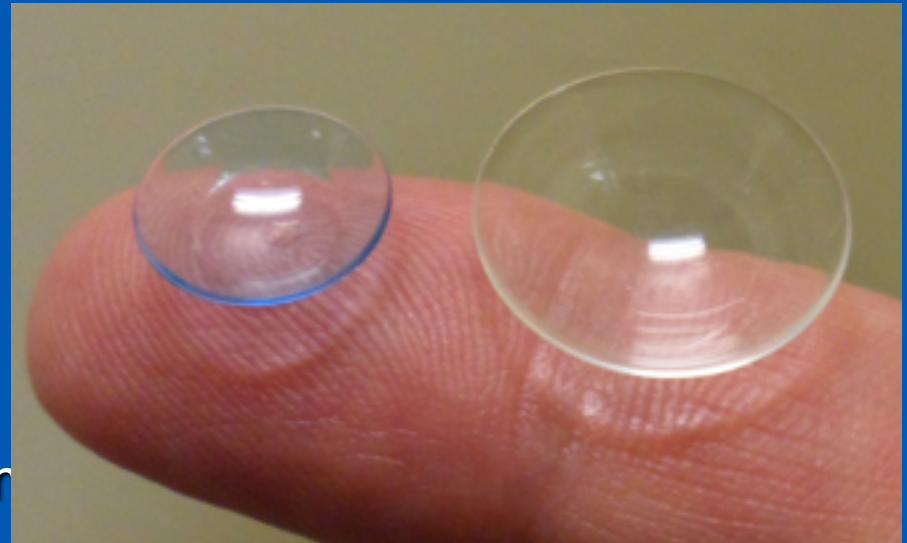
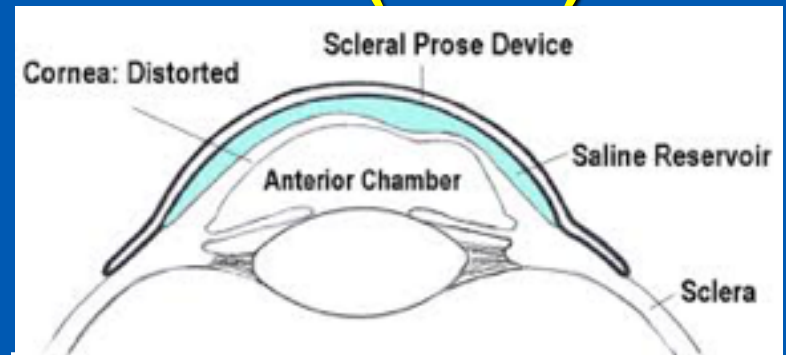
Persistent Epithelial Defect (PED)

- Amniotic Membrane
- Can be used under a contact lens, or to fill the hole with layers of AMT and then a large layer sewn over the whole cornea with a purse string suture.



Persistent Epithelial Defect (PED)

- Scleral Lens Therapy
- Mini-scleral lenses
 - 13-16 mm in diameter
 - Touch the cornea apically or peripherally
 - Easier to fit
- Scleral Lenses
 - 17.5 mm or greater
 - Vault the cornea
- PROSE Lens
 - Custom made 17.5-24 mm



PED – Surgical Treatment

- Surgical Treatment?
 - Epithelial Debridement
 - Conjunctival Flap
 - Limbal Stem Cell Transplant
 - Tarsorrhaphy



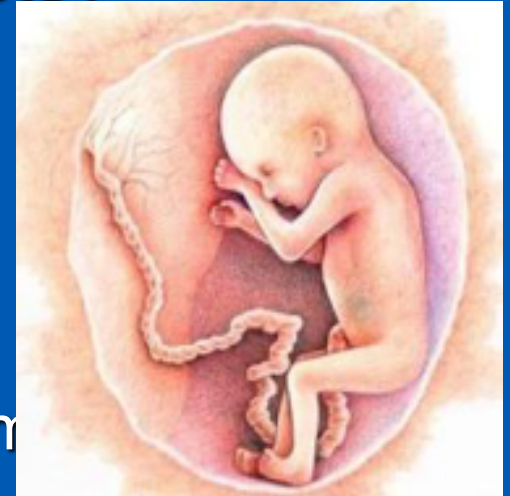
Experimental Alternative Therapies

- Mesenchymal Stem Cells
 - Autologous Adipose – derived
 - Multipotent cells – Umbilical Cord Serum
 - » Capacity to differentiate into any type of human cell
 - Mechanism Unclear
 - » Secretion of trophic factors and cytokines?
 - » Immunomodulation Effects?
 - » Direct differentiation into Corneal Cells?

[Eye Contact Lens.](#) 2014 Jul;40(4):243-7. [Eye Contact Lens.](#) 2014 Jul;40(4):243-7. [Cornea.](#) 2013 Apr;32(4):412-8.

Experimental Alternative Therapies

- Other Whole Blood derived products?
 - Allogenic serum
 - Donated unrelated serum
 - Umbilical cord serum
 - Platelet rich fibrin
 - Platelet rich plasma
 - Purified individual epitheliotrophic component of the serum



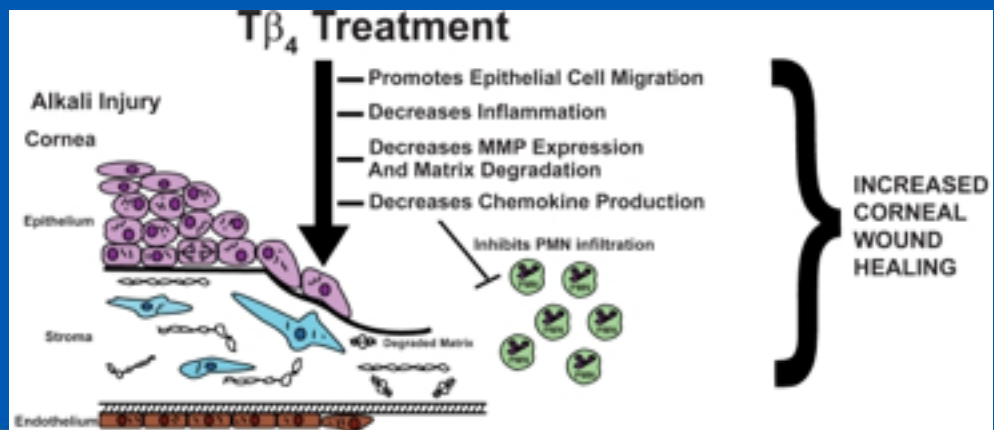
[Jpn J Ophthalmol.](#) 2012 Nov;56(6):544-50.
[Acta Ophthalmol.](#) 2014 Dec;92(8):783-6.

PED- Nexagon

- Compound gel, CoDa Theareuptics
 - Unmodified oligonucleotide that downregulates the key gap junction protein connexin43
- One of the 20 human corneal proteins comprising cellular Gap Junctions
- Potential role in Apoptosis induced by dying cells
- Ormonde S et al. *J Membr Biol.* 2012;245(7): 381-388.

PED - Thymosin β_4

- Protein encoded in the *TMSB4X* gene
- Systematically produced copy of a 43 amino acid peptide found in most human tissues
- Has been shown in corneal wounds to promote re-epithelialization and decrease inflammation

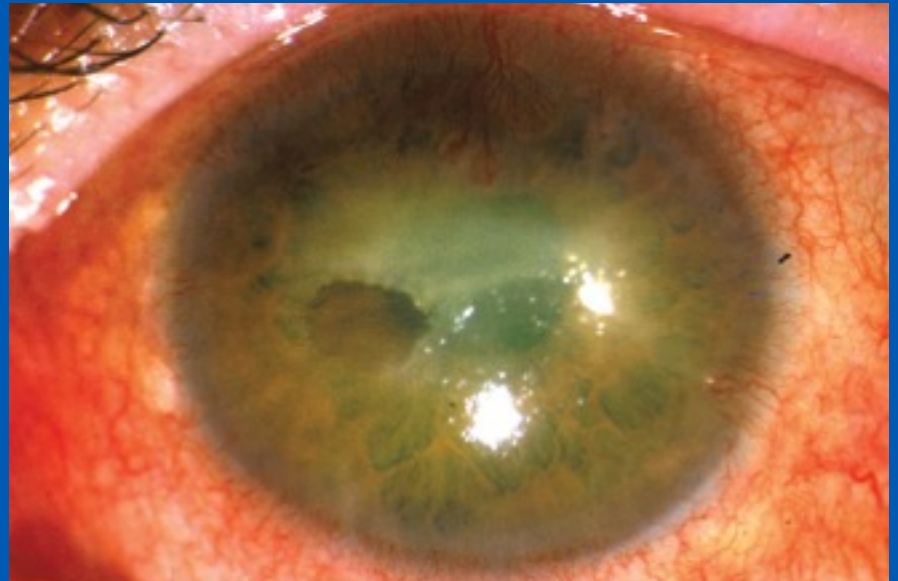


PED- Connexin 43

- Gap Junctions protein
- Connexin43-specific antisense oligodeoxynucleotide was delivered in cold, thermoreversible Poloxamer407 gel under Amniotic membrane or BCL in 5 eyes
- Decreased inflammation in 1-2 days
- PED - healed

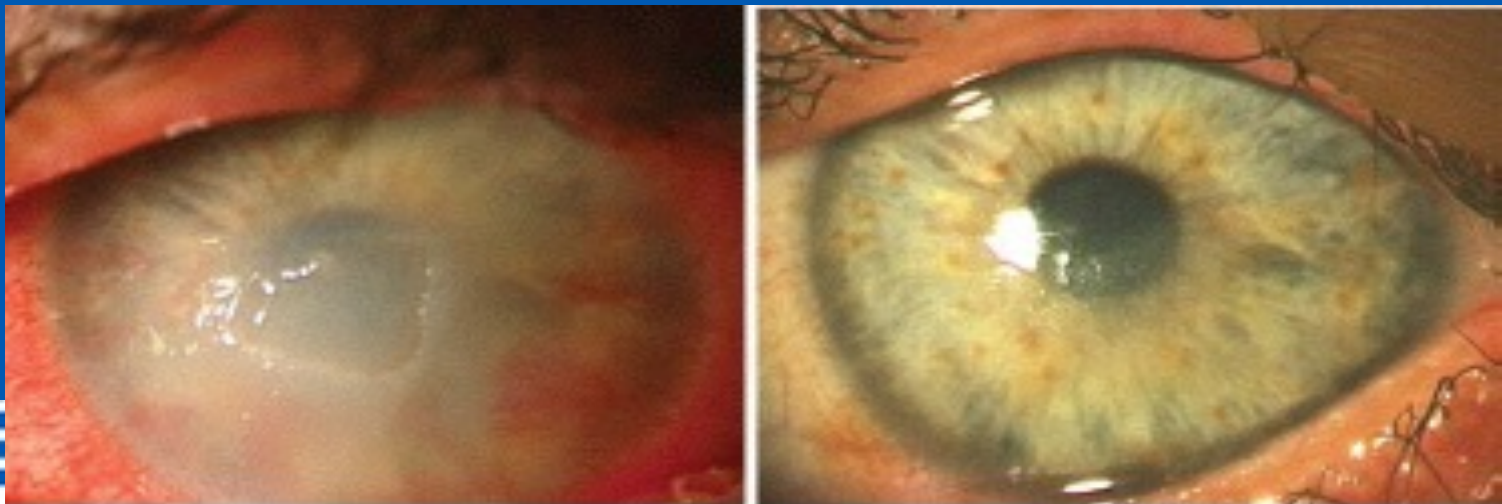
Persistent Epithelial Defects

- Definition
- Medication
- Lubrication
- Occlusion
- Growth Factors



Persistent Epithelial Defect (PED)

- Conclusion
 - Managing PED can be difficult for the MD and Patient
 - Necessary to avoid bad outcomes
 - Early aggressive treatment for high risk eyes
 - When standard medical therapy fails, Surgical options exist



Thank you for your attention

- Questions??
- mmacsai@northshore.org