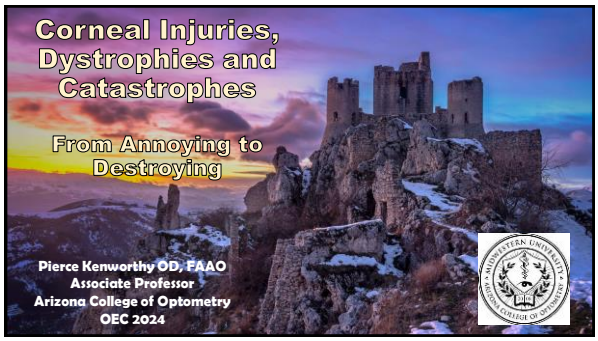


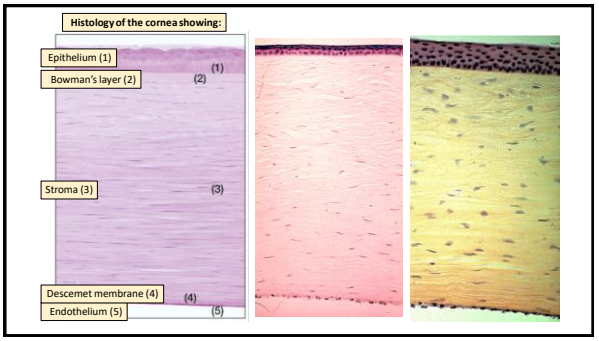

1

## Disclosure Statement

- Nothing to disclose

2

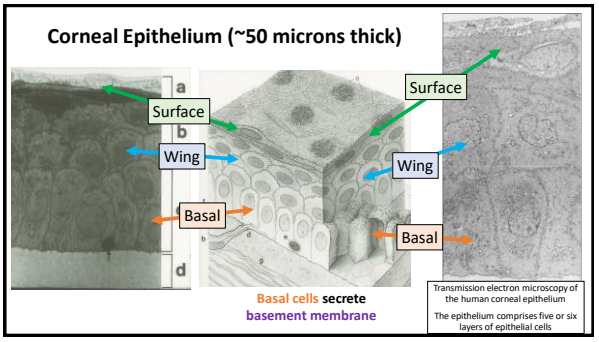
3




4

# Epithelium

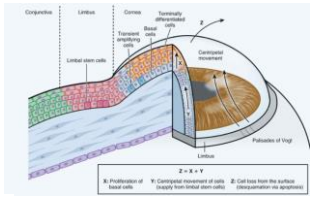
5

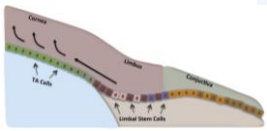



6

## Corneal Stem Cells

Stem cells for the basal epithelium are located in a 1mm band around the periphery (near the limbus)





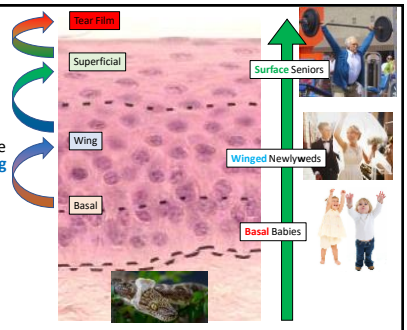
**Turn over time for entire corneal epithelium ~7 days**

7

## Tough Slough

**Differentiation**

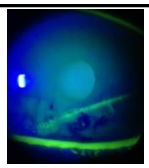
- **Basal cells** differentiate consecutively into **wing** and then **superficial cells**
- Over time the **surface cells *slough*** off and enter the tear film

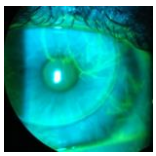



8

## Corneal Wounds

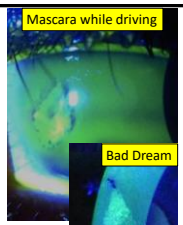
- Injury to the corneal surface is **common** and results in an **epithelial defect**, the rapid resurfacing of which is required for restoration of the continuity of the corneal epithelium
- Among the causes of epithelial defects are:
  - corneal abrasions
  - focal foreign bodies
  - neurotrophic keratopathy
  - sloughing of cells in recurrent erosion

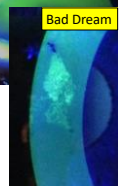


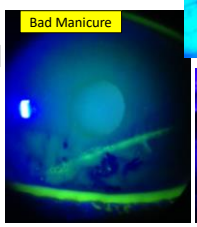


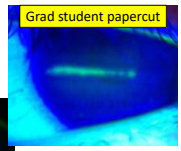
9

## Corneal Abrasions



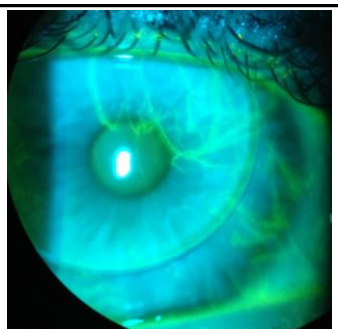





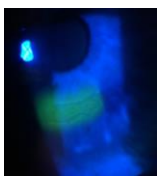
10

## My favorite from contact lens lab



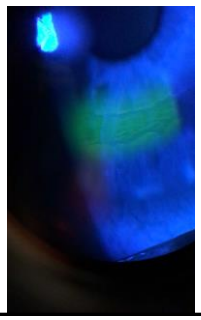
11

36 yo male, his 10 month old daughter scratched his eye 3 hrs ago, 6 out of 10 pain



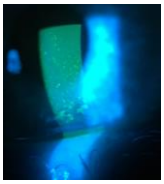
What do you want to do?

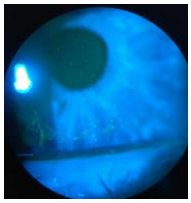
BCL and Polytrim tid w/ AT's

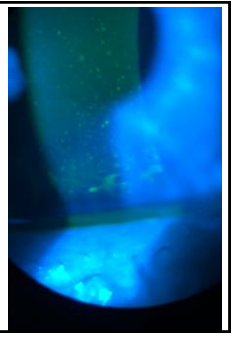


12

1 day f/u after corneal abrasion. Removed BCL







13

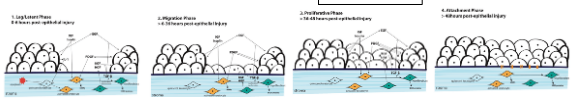
## Healing of the corneal epithelium involves:

Corneal Injury!

sliding of cells to cover the defect

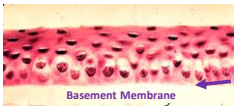
mitosis of cells to restore normal thickness

attachment of cells to the basement membrane



Migration Proliferation Attachment

14



Basement Membrane

- The bottom of the basal cells adheres to the basement membrane via hemidesmosomes
- Hemidesmosomes are linked to anchoring fibrils (*Type VII collagen*)
- *The anchoring fibrils penetrate basement membrane* and form anchoring plaques in the stroma

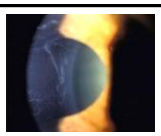
What's easier to staple?

15

# Epithelial Basement Membrane Dystrophy (EBMD)

## Map Dot Fingerprint

16



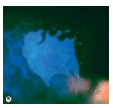
Extra sheets of basement membrane material (1) grow into the epithelium

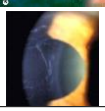
- As basement membrane thickens, the **thickness exceeds the length of the anchoring fibrils**
- Abnormal production of **basement membrane**
  - Extends into epithelium

17

## Map Dot Fingerprint

Abnormal basement membrane produces map and fingerprint changes, and microcysts produce the dot pattern seen clinically





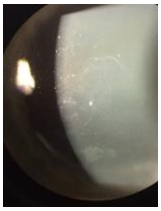
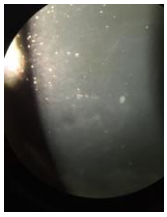
**Map** = extra sheet of basement membrane extending to epithelium

**Dot** = entrapped, migrated cells that become cysts

**Fingerprint** = concentric lines of thickened BM

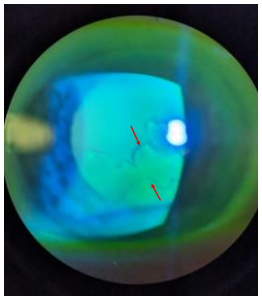
18

2020 - Reduced VA 20/30+ in this 84 year old male OS


19

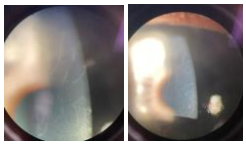
Note the negative staining at the edge of EBMD lesions



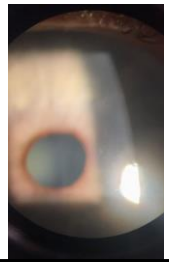
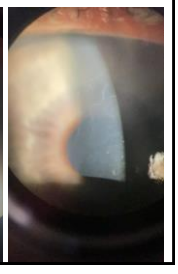
20

## EBMD Symptoms

- Usually asymptomatic
- Rarely have distortion of vision
  - Unless central corneal involvement

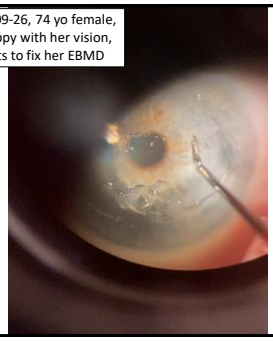
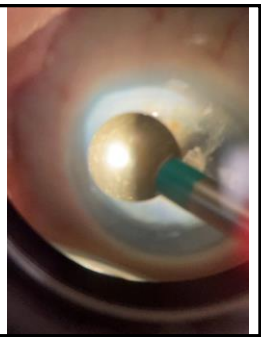



2023-06-15, 73 yo female referred for dry eye. BCVA 20/30 OU. Has visual ghosting and lots of glare at night.

21

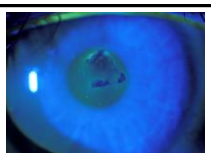
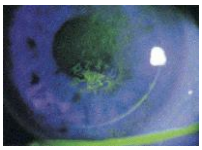
2023-09-26, 74 yo female, unhappy with her vision, wants to fix her EBMD

22

**EBMD may predispose patient to recurrent corneal erosion** (RCE)

- Lack hemidesmosome between basal epithelial cells
- Abrupt onset severe pain
  - Usually at night or first thing in A.M.

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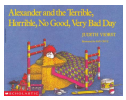
## Recurrent Corneal Erosions

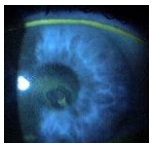
When cells don't stick


24

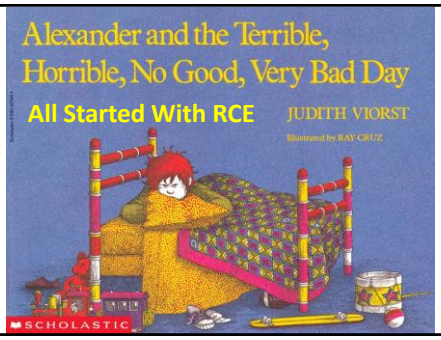
## Recurrent Corneal Erosion

- Due to **weakly adherent corneal epithelium** resulting in intermittent occurrences of **spontaneous epithelial defects**
- Episodes are characterized by sudden onset of eye pain, **typically upon waking in the morning or during the night**, with associated symptoms of tearing, redness and photophobia
- The pain ranges from ***mild to severe***, and the length of episodes can vary from ***minutes to days***



25




26

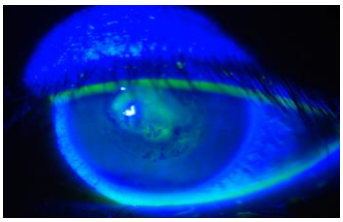
All in a Saturday's work

32 yo female calls the emergency line on **Saturday,** says she felt **terrible pain upon awakening and opening eye**.

Has had similar episodes in past, causes anxiety when waking up.

Hx of corneal abrasion

BCL and recommended corneal scraping



Recurrent corneal erosion

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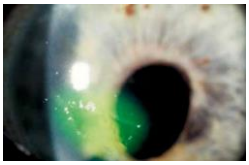
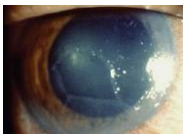
## Treatment of Recurrent Corneal Erosion

Depends on severity, but may include:

- Artificial Tears
- Antibiotic
  - Erythromycin ung qid
  - Vigamox qid
- Bandage CL
  - May need to debride loose tissue first
- Cyclopentolate 1%
- NaCl 5% (Muro 128)
- Oral analgesics as needed





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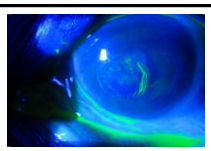
## Recurrent **Recurrent** Corneal Erosions

- For unresponsive patients, other therapies include **systemic tetracyclines** (eg, doxycycline 50 mg BID *x 2-3 months*) and **topical corticosteroids**.
- Each drug class prevents breakdown of collagen and hemi-desmosomes by inhibiting the production of MMP-9.

Clin Ophthalmol. 2019; 13: 325–335.
Published online 2019 Feb 11. doi: 10.2147/OPTH.S157430

Recurrent corneal erosion: a comprehensive review

Darby D Miller,[1] Syed A Hasan,[1] Nathaniel L Simmons,[2] and Michael W Stewart[3]

Slit lamp appearance of active recurrent erosion showing ragged, edematous, disrupted gray epithelium

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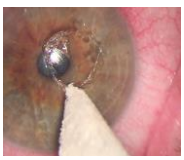
## RCE Surgical Management

- Anterior stromal puncture
  - Risk of stromal scarring
- **Debridement** and polish
- **PTK** (phototherapeutic keratectomy)




30

## Diamond Burr Polish for RCE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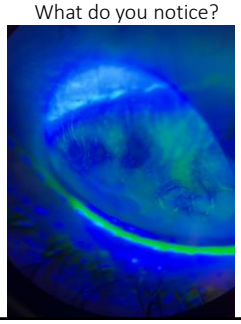
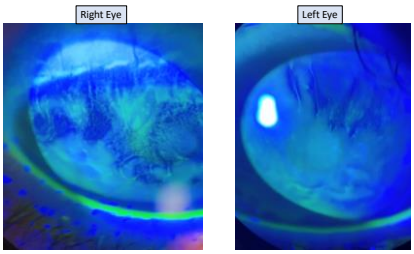
What do you notice?



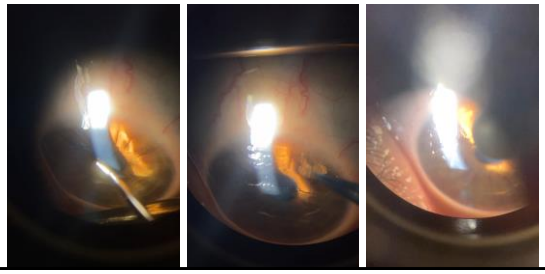
2023-03-28, patient who had SMILE 1.5 yrs ago. Has been dealing with dry eye since. Reports ***fear of opening eyes*** and never knowing if it will cause pain or not. Eyelids also swell when it happens

32




33

2023-04-04, anterior keratectomy procedure. Debridement and diamond burr polish



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Appearance immediately after procedure

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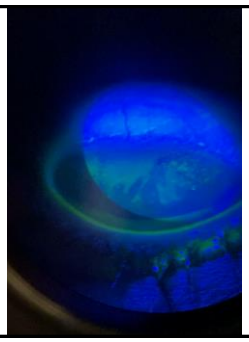
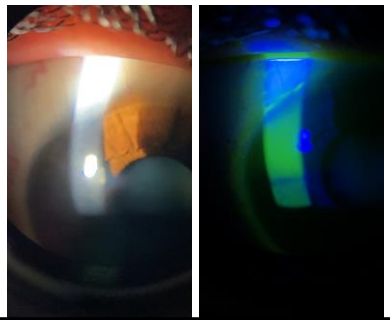
2023-04-11, one week later, time to remove BCL and take a look



36

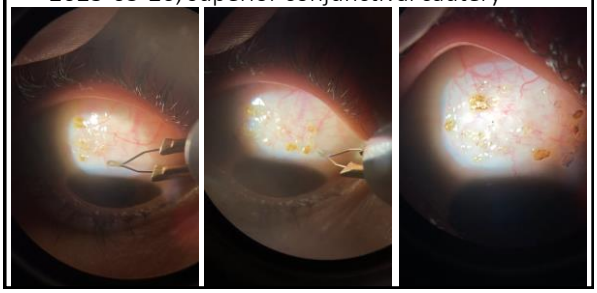
2023-05-02, one month follow up.

Still experiencing ***some stickiness under lid***, but has improved.



37

2023-05-26, superior conjunctival cautery



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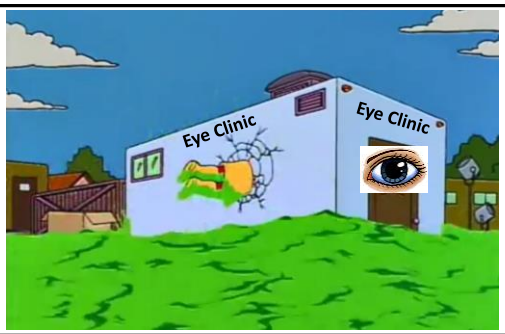
# Chemical Injuries

39

**My Eyes! The Goggles Do Nothing!**

40




41

"The best result that can be obtained in an eye after a severe alkali burn is a totally vascularised and scarred cornea that has not undergone ulceration and in which glaucoma has not developed"
*Pfister 1983*[1]

- Ocular chemical injuries are **true ophthalmic emergencies** due to the potential for permanent corneal and intraocular damage leading to visual impairment or even blindness
- Although the final visual outcome is strongly related to the severity and nature of the initial chemical exposure, the ***prognosis is very heavily influenced by the timing*** of appropriate **treatment**

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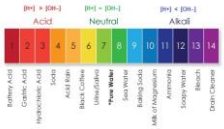
# Acid or Alkali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# Acid or Alkali

Sodium hydroxide


44

# Acid or Alkali

Acetic acid


45

# Acid or Alkali

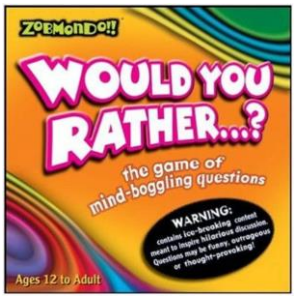
Sulphuric acid


46

# Acid or Alkali

Calcium hydroxide


47




WOULD YOU RATHER...

Lick a dirty trash can or the bathroom floor?

WOULD YOU RATHER...

Have one eye in the middle of your head or two noses?

48

# Ocular Penetration

**Alkalis characteristically penetrate the eye more rapidly** than acids and typically cause the most severe chemical injuries

However, **very strong acids** may penetrate as rapidly as alkalis and studies have shown ***no clinically significant differences*** in clinical course and prognosis between severe acid and alkali burns


Corneal alkali burn

**Figure 5-5** • Alkali burn demonstrating corneal burns and conjunctival injection on the day of the accident.


Corneal alkali burn

**Figure 5-6** • Complete corneal tissue destruction 7 days after alkali burn.


49

## Injury, Repair and Differentiation of Ocular Surface

**Cornea**
- Recovery from epithelial injury is dependent on the **centripetal migration of cells** from the most proximal region of viable epithelium

**Limbus**
- Epithelial defects involving a portion of the cornea are ***replenished by adjacent corneal epithelium*** while complete corneal epithelial defects rely on the ***limbus*** for re-epithelialization

**Conjunctiva**
- The **conjunctiva is the only source** of regenerating epithelium in the event of ***complete corneal and limbal epithelial loss***

A severe, secondary, microbial corneal stromal abscess complicating a chemical eye injury

Nonhealing corneal epithelial wounds pose a significant risk as they expose the cornea to potential microbial infection

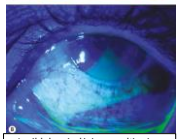

Trichiasis occurring as a sequela of a combined thermal and chemical injury.

50

2020 - 38 yo female from Guatemala, 9 yrs ago was cleaning toilet, and **bleach** splashed in her right eye
(*Pt lost her cosmetic contact in shower yesterday, and was emotional about going to work like this*)

51

Examples of mild, moderate, and severe chemical injuries



A mild chemical injury resulting in a focal corneal epithelial and conjunctival defect with associated conjunctival hyperemia

A moderate chemical ocular injury resulting in three clock hours of limbal ischemia.

A severe chemical injury with marked, diffuse limbal and conjunctival ischemia and corneal edema.

52

# Management of Chemical Injury

EMERGENCY ALERT

**OPHTHALMIC EMERGENCY**

- Immediate copious irrigation with sterile water, saline, or Ringer's solution.
- Measure pH before and after irrigation, continue irrigation until pH is neutralized.
- Remove any chemical particulate matter from surface of eye and evert lids to sweep fornices with sterile cotton swab.

53

## Role of Inflammation

- Chemical injury to the eye is associated with a **profound release of pro-inflammatory mediators** and the infiltration of inflammatory cells into injured tissue
- **Regulation of this inflammatory response is crucial**

Review Article | Published: 22 June 2020

**Chemical eye injury: pathophysiology, assessment and management**

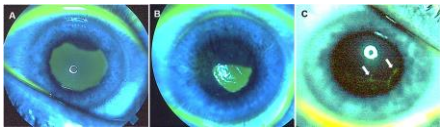
Topical corticosteroids are the mainstay of treatment for controlling the acute inflammatory reaction of chemical eye injury

Potent corticosteroids such as ***dexamethasone 0.1% and prednisolone acetate 1%*** are common choices

General consensus is to ***taper the dose or frequency of topical steroids after 7–10 days*** (because they can inhibit wound healing and collagen re-formation)

54

Epithelial defects warrant the use of a **topical antibiotic** for antimicrobial prophylaxis




**a** Central epithelial defect with intact limbus is shown.

**b** Healing is occurring with centripetal migration of epithelium. The defect assumes a trianglar shape.

**c** Final closure of the defect with 'contact lines' resembling a pseudodendrite (*arrows*).

***Broad-spectrum antibiotics*** are used for prophylaxis, to reduce the load of commensal flora that may occur with necrotic tissue or to treat frank infection

Review Article | Published: 22 June 2020

**Chemical eye injury: pathophysiology, assessment and management**

Eye 34, 2001–2019 (2020) | Cite this article

55

2022-10-11, 76 yo male got bleach in his eye two days ago, was wearing scleral contacts when it happened. Now reports cloudy vision and a red eye.

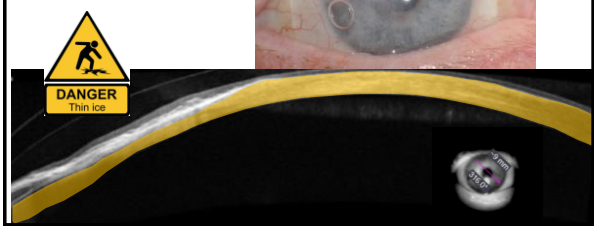
56

2022-10-11, What will you do?

- Sent to corneal specialist
  - Moxifloxacin q1h
  - Tobramycin q1h
  - Pred acetate qid
- Cornea melted
  - Prokera
  - Then **conjunctival graft** with amniotic membrane
- Fast forward 9 months

57

2023-07-03, post reconstruction with conjunctival flap (*bubble under scleral lens*)

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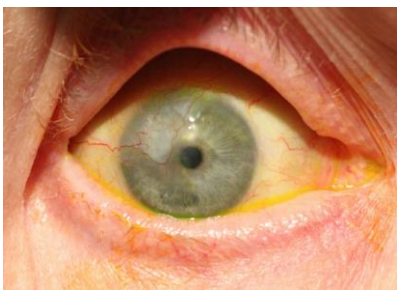
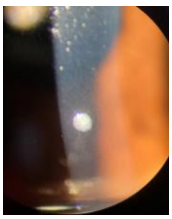
2023-09-13

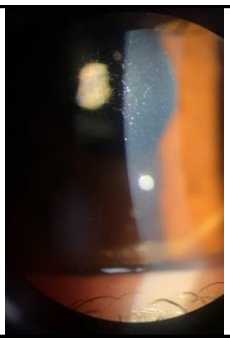
Still stable



59

2023-04-26, 19 yo male who cleans pools and two days ago while handling **chlorine tablets** the wind blew some into his face, and eyes immediately became irritated. Tried to rinse it out with the hose and then shower afterwards. When looking in the mirror ***can see something on his right eye***. Does not wear CL.



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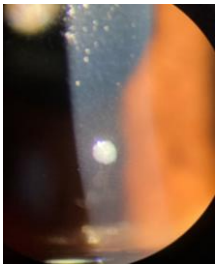
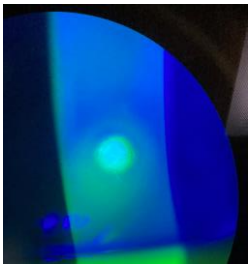
What's the staining like OD?

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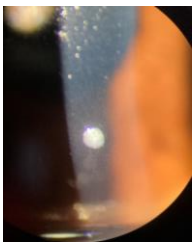
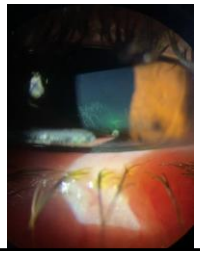
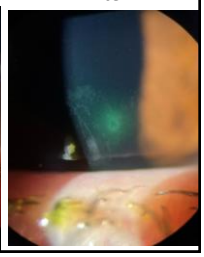
Before

After



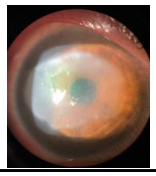
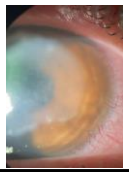
62

**What does your gut say this is?**

37 yo female contact lens wearer

63

2023-05-19, 37 yo female presents with eye irritation, redness, and blurry vision OD. Pt thinks she **got something in her eyes** last Tuesday (possibly cat hair?). Irritation continued Wednesday, so pt went to **urgent care** last Thursday and was given **ketorolac** 0.5% QID and **Ciprofloxacin** 0.3% q6hours, **and she was also given a bottle of proparacaine to use for pain.** Because her eyes were swollen and irritated, she **couldn't get her contacts out** for three nights/three days, Wednesday-Thursday-Friday before she could remove them on Saturday morning. Yesterday the blurry **vision got worse** and started to see a **white area on her right eye**. Saw OD and was given new eye drops **Moxifloxacin** q1h and **polymyxin B-trimethoprim** QID and AT prn.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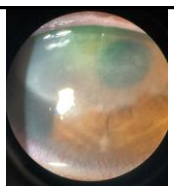

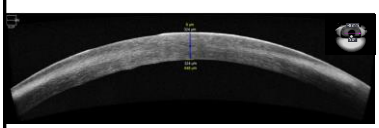

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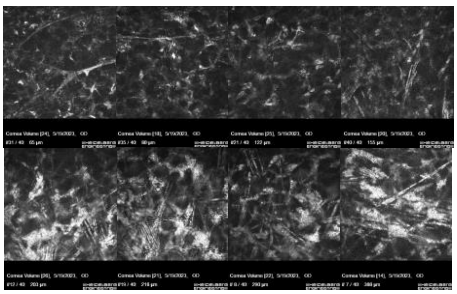
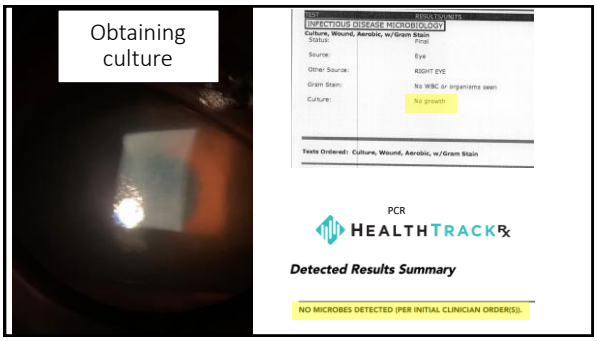


No evidence of acanthamoeba or fungus on confocal

66

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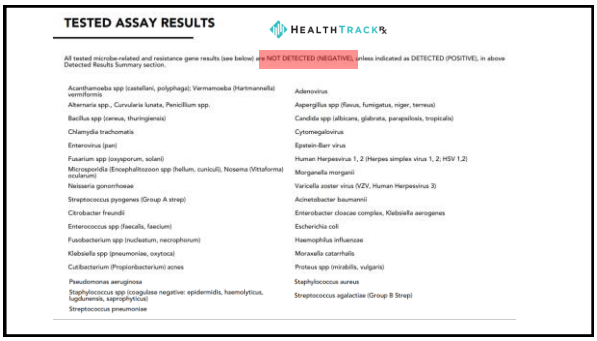


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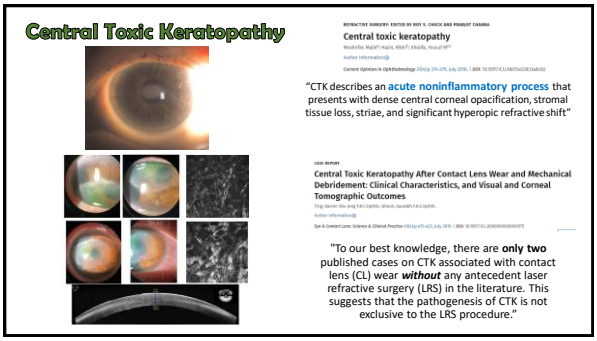


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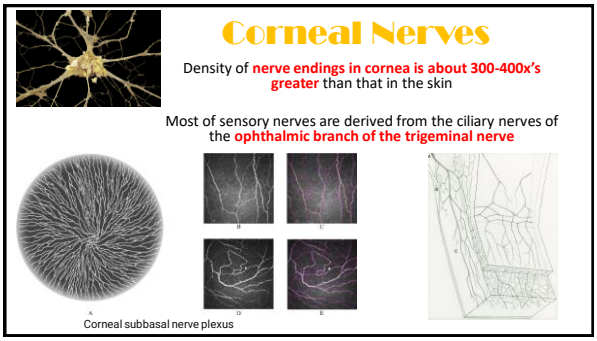


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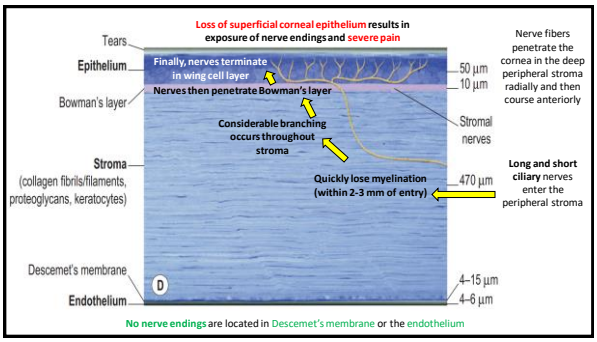


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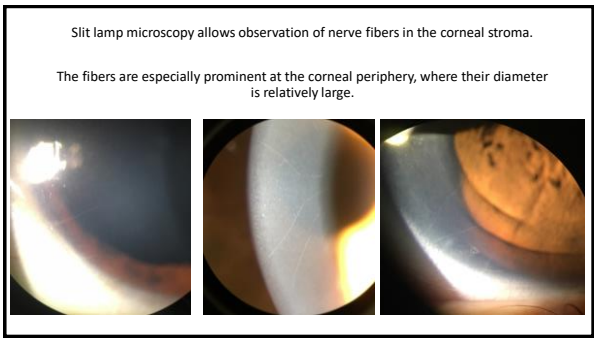


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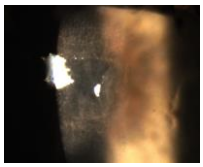
## Neurotrophic Effect on Cornea

- Corneal nerves influence corneal metabolism and aid in tissue maintenance
- Individuals with corneal anesthesia and a loss of nerve endings may have…
  - **Increased epithelial permeability**
  - Reduced mitosis
  - **Decreased cell adhesion**
  - Impaired wound healing
- **Loss of corneal sensation often results in breakdown of corneal integrity**



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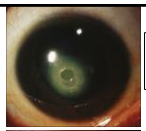
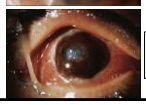
## Neurotrophic Keratitis

- Neurotrophic keratitis is a degenerative disease of corneal epithelium characterized by **impaired healing**
- **Absence of corneal sensitivity** is the hallmark of the condition, which may end in corneal stromal melting and perforation.
- Cornea becomes **prone to injury** and corneal **healing rate is decreased**
- Leads to formation of **nonhealing epithelial defects**
- The most common causes of corneal anesthesia are **herpes simplex (HSV)** and **herpes zoster (HZV)** virus infections of the ocular surface



Central, circular, punched-out epithelial defect secondary to and classic for neurotrophic keratitis

Thinning in a cornea that suffers decreased sensation

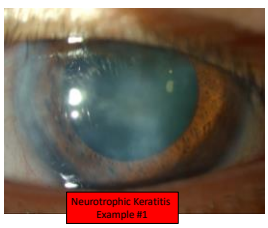


Complete corneal necrosis secondary to topical anesthetic abuse

74

**Neurotrophic Keratitis Secondary to Herpes Simplex**

41 yo male patient with recurrent herpes simplex infection in cornea (specifically has disciform keratitis). Should we check corneal sensation?



Neurotrophic Keratitis Example #1

75 yo female patient diagnosed with herpes simplex 2 weeks ago Epithelial dendrites resolved with Viroptic, but now has large, non-healing epithelial defect…

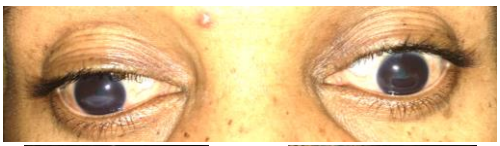
"Oh, **but my eye feels fine**, I just can't see"

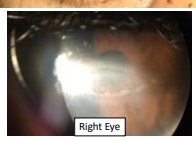
Neurotrophic Keratitis Example #2

75

Neurotrophic Keratitis Example #3

2020-11-05, 39 yo male, pt arrives to clinic for blurry vision. Was seeing 20/400. ***Eyes feel fine though.*** Diabetes seriously uncontrolled





Right Eye

Left Eye

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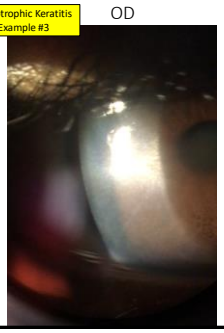
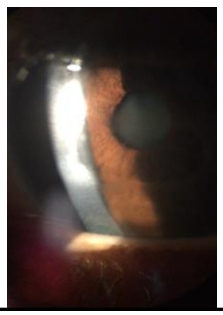
Neurotrophic Keratitis Example #3

OD



OS



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Neurotrophic Keratitis Example #4

2022-02-04, 47 yo diabetic male with neurotrophic keratitis, here for 1 week lateral tarsorraphy post-op OU

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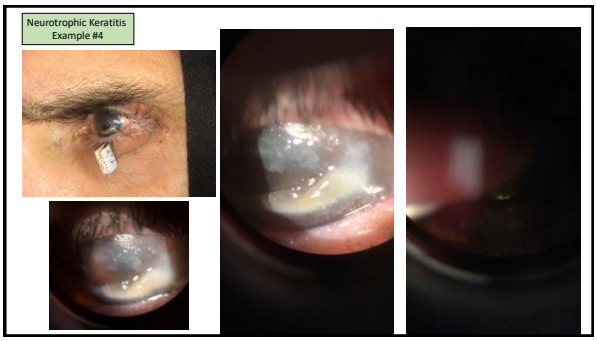


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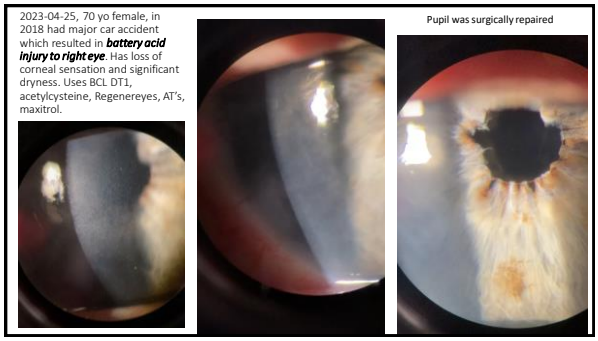


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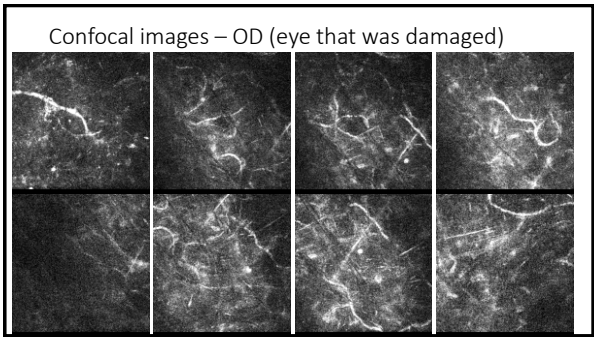


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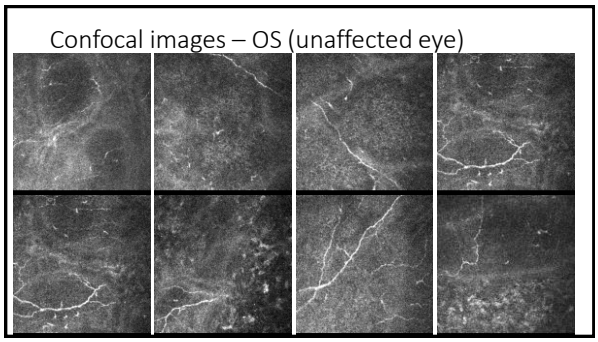


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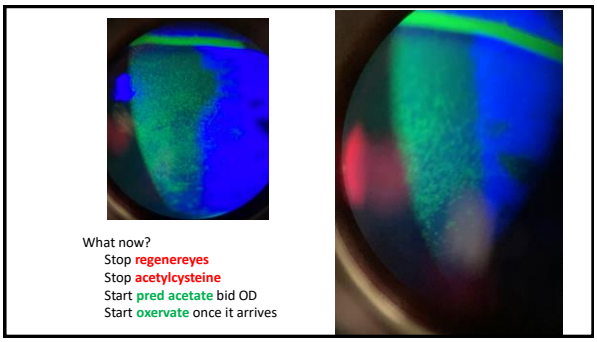
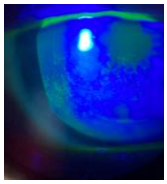
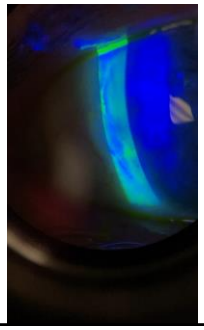



84

2023-06-29, today is patient's last day of her 8 week course of oxervate. Feeling much better





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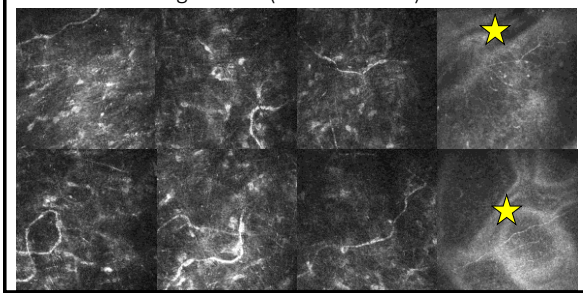
Confocal images – OD (after oxervate)



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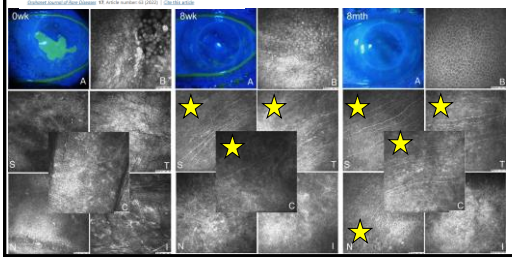
**Eight months follow-up of corneal nerves and sensitivity after treatment with cenegermin for neurotrophic keratopathy**

"There was significant corneal nerve regrowth especially in the peripheral cornea: centripetal progression starting at 8 weeks and significant branching starting at 2 months"




"Progressive nerve regrowth was accompanied by a gradual increase in branching over time"[5]

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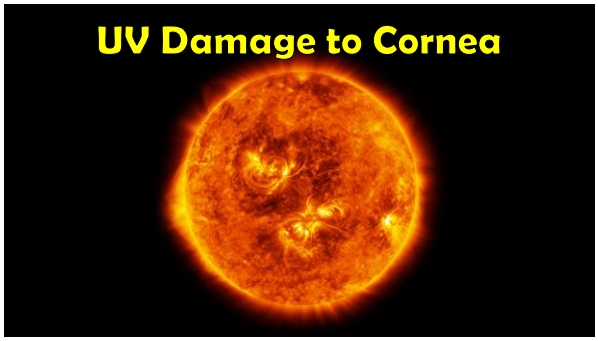


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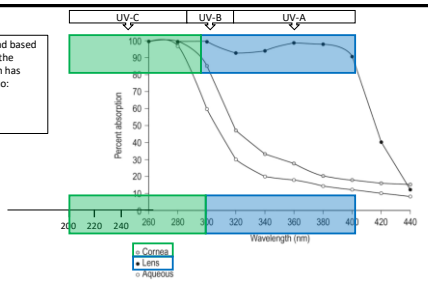
For convenience, and based on biologic effects, the ultraviolet spectrum has been subdivided into:
UVC (200–290 nm)
UVB (290–320 nm)
UVA (320–400 nm)




The wavelengths between 200 and 300 nm are strongly absorbed by the cellular elements in the cornea

The wavelengths from 300 to 400 nm are *transmitted by the cornea* and absorbed by the lens

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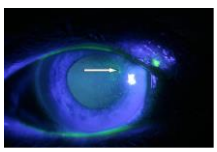
## Ultraviolet Radiation (UVR)

- The corneal **epithelium** is the ***first tissue layer*** exposed to incoming light and consequently shows the **most absorption and tissue damage from UVR**
- The ability of the cornea to absorb short wavelengths is **protective** to deeper structures (lens and retina).....but it's "***dangerous***"
- Possible outcomes with moderate UV exposure in primates:
  - separation of superficial epithelial cells
  - nuclear and cytoplasmic damage in the remaining attached cells



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# Clinical Comment:

## Photokeratitis

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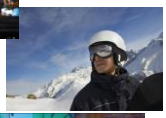
## Photokeratitis

- The most common types of human UVR injury are:
  - welder's keratitis
  - snow blindness
  - keratitis after exposure to tanning sunlamps
- Similar to findings in animal studies, the **acute effects of UVR in humans are generally delayed for 8 to 12 hours after exposure**
- Early symptoms include generalized ocular surface discomfort, followed by pain, photophobia, and foreign body sensation
  - Individuals suffering from this condition can report intense discomfort



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Manfred Mann singing about how acute overexposure of UV can lead to painful, blinding photokeratitis

"Blinded by the light
Revved up like a deuce
Another runner in the night"



93

94

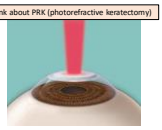
# Bowman's

95

## Bowman's layer


Sir William Bowman (1816-1892)

- The second layer of the cornea
  - About 10 µm thick (8-14)
- NOT a true membrane, actually a **random arrangement of collagen** fibrils and **proteoglycans**
- **Bowman's layer does *not* regenerate after injury**
  - Recent clinical experience with excimer laser photoablation demonstrates that a **normal epithelium** is formed and maintained even in the **absence** of Bowman's layer
- Unsure if it's necessary, in fact *many mammals don't even have Bowman's layer (rodents for example)*
- **But it is resistant to damage and has strong tensile strength**




96

## Alger Brush for Foreign Body Removal



97

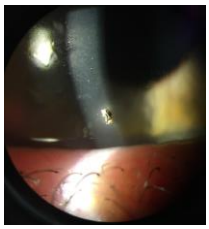
## Bowman's and Alger Brush


Alger brush burrs are widely reported as having a "***pressure-sensitive clutch***" that will prevent the mechanism from penetrating Bowman's membrane

**However**, if the foreign body itself is penetrating Bowman's membrane, there is no longer an effective resistance to initiate the stop, which can lead to wide scarring if used aggressively

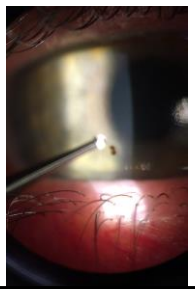
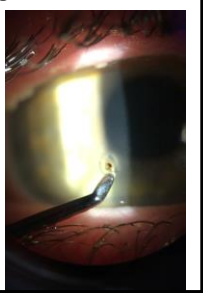
98

2019-11-08, Friday 4:00pm got a call from front desk that an emergency patient was added to schedule. Metal foreign body? On his way…
26 yo male arrives at 4:40pm




99

## Don't be a Butterfinger

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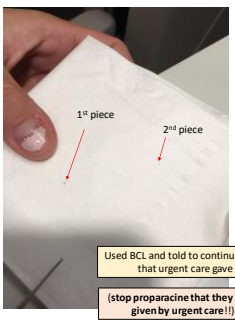
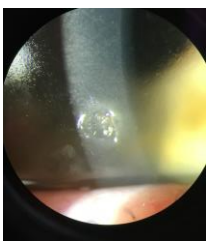



## No more rust or metal



101

# Stroma

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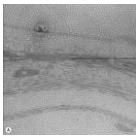
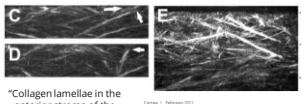
## Corneal Stroma

- Thickest layer of the cornea, accounts for 90% of the thickness or about 500 microns
- Contains **collagen**, **keratocytes**, and **ground substance**
- Stroma must be organized so that light can pass through easily
- The collagen fibrils form flat organized bundles called **lamellae**
  - There are 200-300 lamellae total
- The spacing of the fibers within the lamellae is very regular






"Collagen lamellae in the anterior stroma of the normal human cornea are ***interwoven in three dimensions*** and adhere densely to Bowman's layer"

Cornea · February 2017

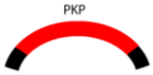
**Three-Dimensional Analysis of Collagen Lamellae in the Anterior Stroma of the Human Cornea Visualized by Second Harmonic Generation Imaging Microscopy**

103

## Corneal Collagen Fibers in Clear Cornea

104

## PKP

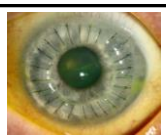



## Penetrating Keratoplasty

Penetrating keratoplasty (PK) is a transplant procedure in which full-thickness, host corneal tissue is replaced with donor corneal tissue

Over the past decade, there has been a trend away from PK toward ***partial-thickness*** corneal procedures, with the goal of only replacing the diseased corneal layer and maintaining the integrity of any normal corneal anatomy

105



## DALK


## Deep Anterior Lamellar Keratoplasty

Anterior lamellar keratoplasty is a technique whereby the diseased corneal stroma is partially or totally replaced by donor tissue, provided the endothelium is still healthy

Anterior lamellar keratoplasty is becoming the preferred procedure for advanced keratoconus, stromal dystrophies, and partial-thickness corneal scars when they cannot be treated with excimer laser procedures

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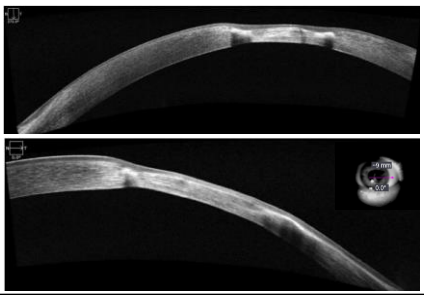
## Examples of Indications for DALK

- Ectatic disorders
  - keratoconus, keratoglobus, pellucid marginal degeneration
- Scars
  - traumatic, surgical, chemical injury, herpetic (simplex and zoster), post-bacterial ulceration, trachomatous scars, post-fungal ulcers, and other superficial scars
- Dystrophies
  - epithelial, Bowman's membrane, Reis–Bücklers dystrophy, map-dot-fingerprint dystrophy with recurrent erosions, and stromal dystrophies
- Degenerations
  - Salzmann nodular degeneration, climatic degeneration, band keratopathy

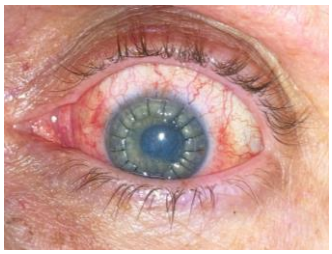
107

67 yo female, before surgery – corneal scar and thinning from prior herpes



108

2023-10-27, 67 yo female, 1 day post op DALK, hx of herpetic corneal scar

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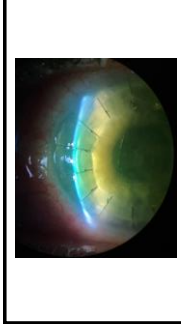
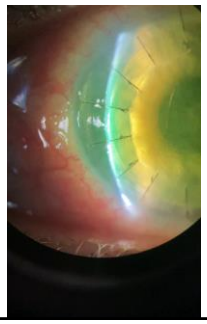
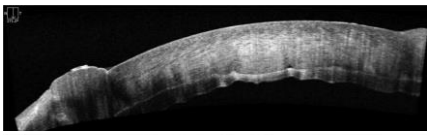
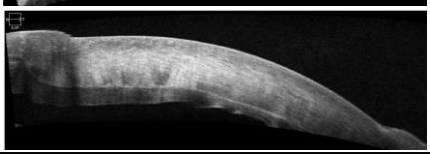



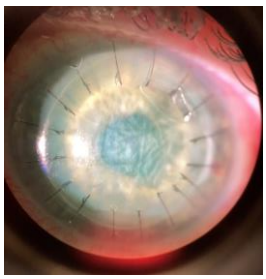
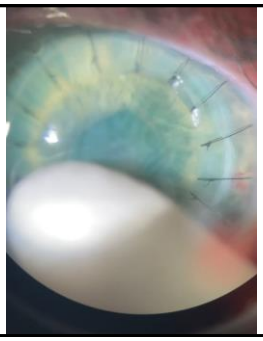

110

After DALK – one day post op

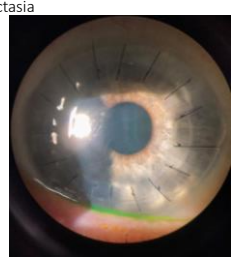
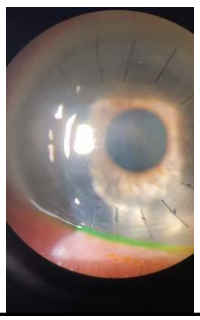
111

Placed BCL on for comfort….what about bubble?

112

2023-09-01, 67 yo female, one month post op DALK for corneal ectasia

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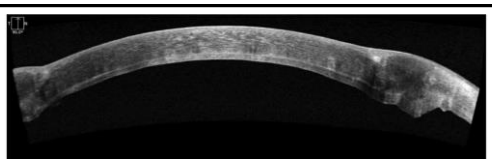
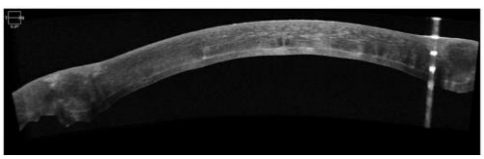

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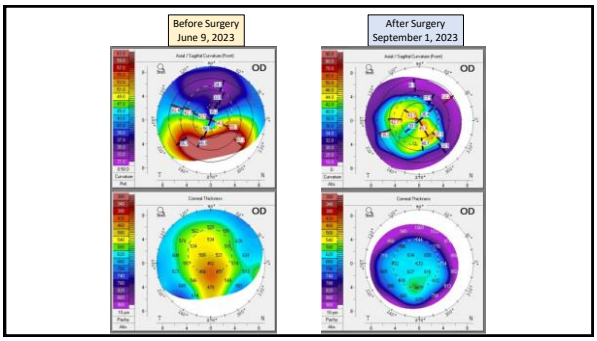


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# Keratoconus

Contact Lens and Anterior Eye
Keratoconus: An updated review

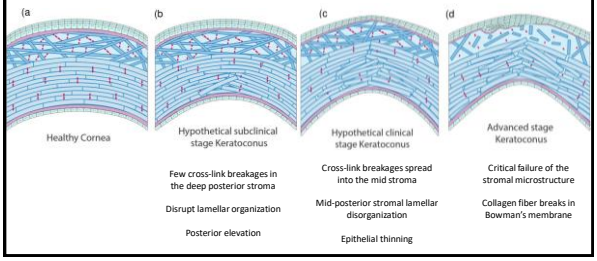
- The well-organized architecture of the corneal stroma is ***compromised*** in keratoconus
  - **Reduction** in the ***number*** of lamellae
  - Collagen **lamellae are expanded** in association with protrusion of the cone
  - **Lamellar splitting** into multiple bundles of collagen fibrils
  - **Loss** of anterior lamellae

116

## Biomechanics of keratoconus: Two numerical studies

Nicolas Falgayrettes, Etienne Patoor, Franck Cleymand, Yinka Zevering, Jean-Marc Perone
Published: February 2, 2023 • https://doi.org/10.1371/journal.pone.0278455

Blue bars/bricks = lamellae
Red dashes = interlamellar cross-links (*generated by ground substance*)

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## My in-laws favorite movie

https://www.youtube.com/watch?v=tcR7LgBVTNE



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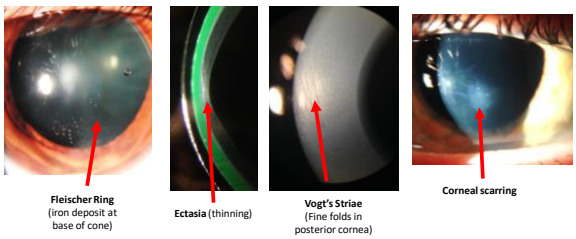
## Corneal Findings Related to Keratoconus



**Fleischer Ring** (iron deposit at base of cone)

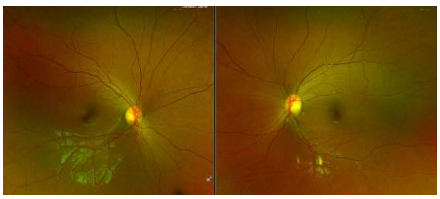
**Ectasia** (thinning)

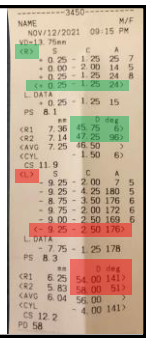
**Vogt's Striae** (Fine folds in posterior cornea)

**Corneal scarring**

119

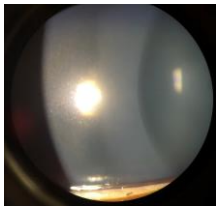
2021-11-12, 24 yo female w/ **gradually reduced VA OS.**
Today difficult refraction, **BCVA 20/30 OS**
Last doctor told her she has **"lazy eye" OS**





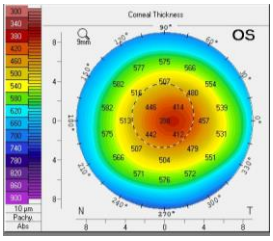
120

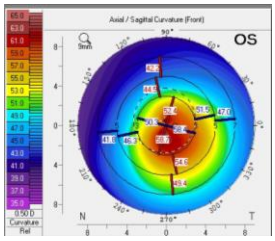
Can you see the Fleischer Ring?



121

Corneal thinning and steep cone consistent with keratoconus

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# CXL

## Corneal Crosslinking

Crosslinking can be defined as the creation of bonds that connect one polymer chain to another

CXL strengthens corneal tissue by utilizing riboflavin (vitamin B2) as a naturally occurring photosensitizer and Ultraviolet-A light (UVA) to release free radicals that increase the formation of intra- and inter-fibrillar carbonyl-based covalent bonds through the process of photopolymerization

Although the major indication for the use of CXL is to arrest the progression of KCN it has also been utilized in the treatment of pellucid marginal degeneration and iatrogenic ectasia resulting from LASIK, photorefractive keratectomy (PRK), and radial keratotomy

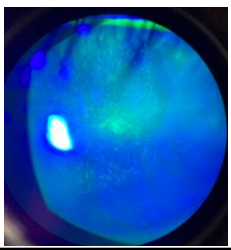
123

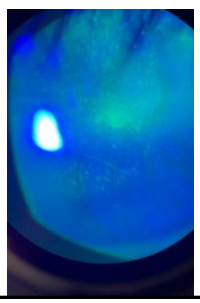
Epithelial removal before CXL

- 9mm diameter epithelial removal
- First, 0.1% Riboflavin 20% Dextran solution
- Then soak with riboflavin without dextran
- Apply 30min UV exposure

124

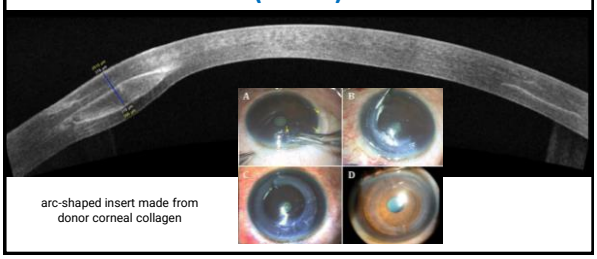
47 yo male, 1 week post CXL, after removal of BCL





125

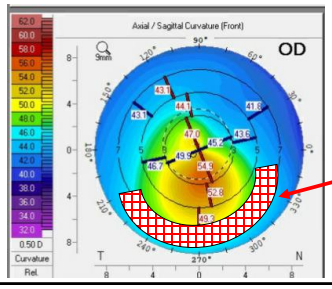
## Corneal Allogenic Instrastromal Ring Segment (CAIRS)



arc-shaped insert made from donor corneal collagen

126

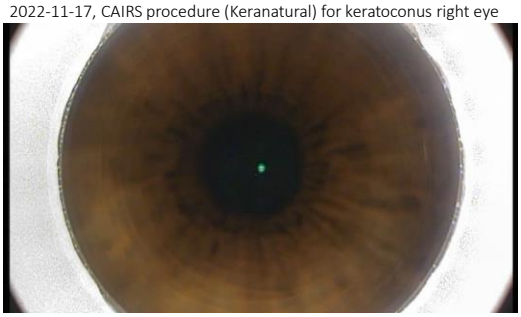
2022-08-17, 55 yo male patient with keratoconus.
Pre-Op Pentacam




Can something be used to provide support around cone?

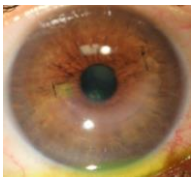
127

2022-11-17, CAIRS procedure (Keranatural) for keratoconus right eye



128

2022-11-18, one day post op OD



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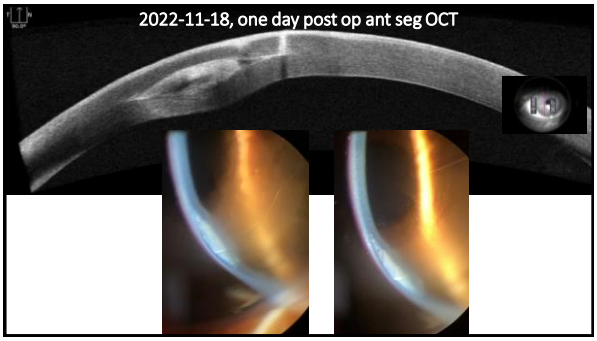


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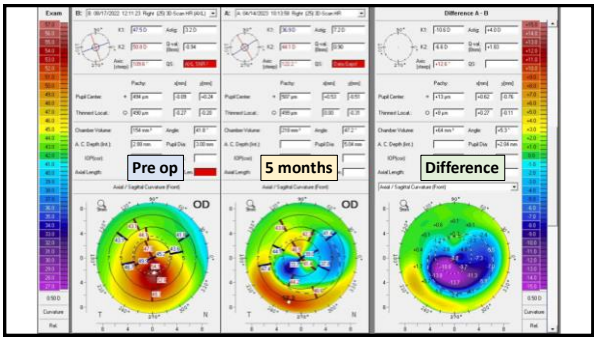
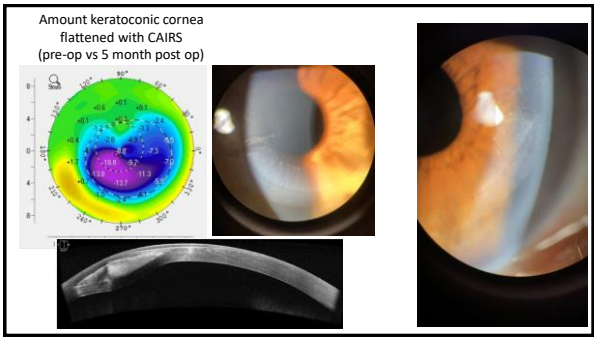



131

Amount keratoconic cornea flattened with CAIRS
(pre-op vs 5 month post op)



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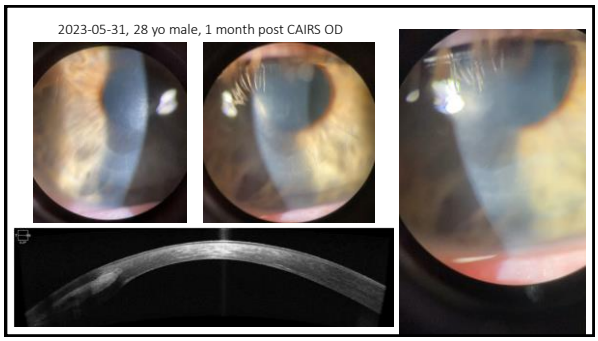


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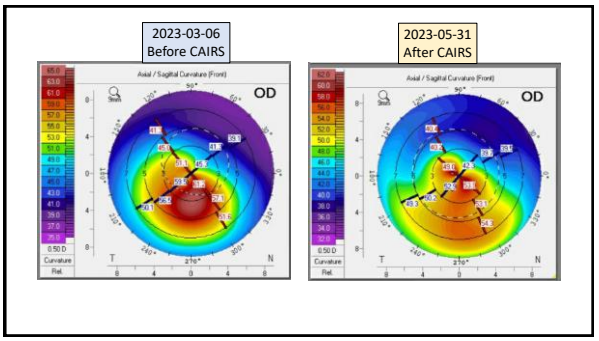


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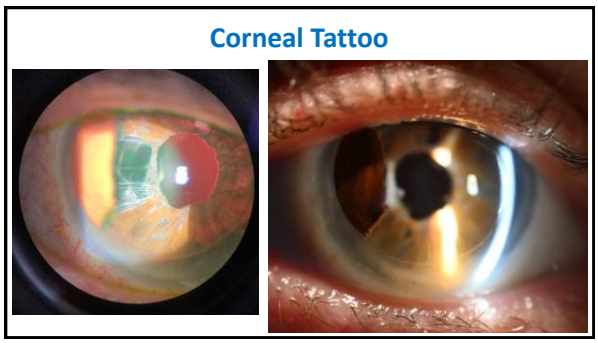


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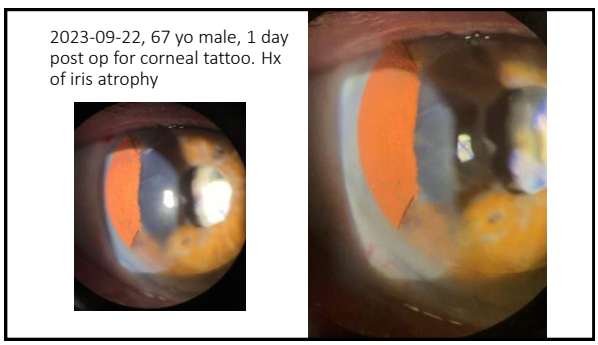
136

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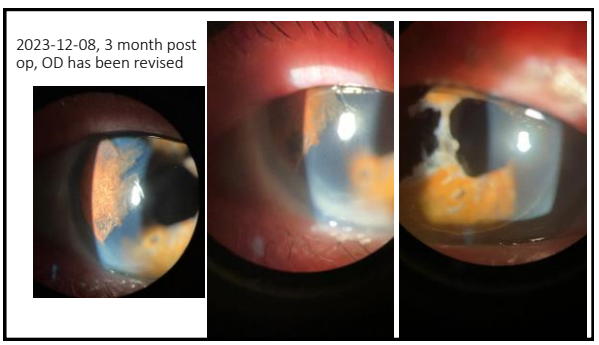


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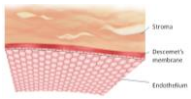
# Descemet Membrane

139

## Descemet Membrane

Endothelium's Basement Membrane


- The basement membrane of the corneal endothelium
- **Always being produced**
- Gradually increases in thickness from birth (3 µm) to adulthood (8–10 µm) in humans
- The Descemet membrane adheres tightly to the posterior surface of the corneal stroma and reflects any change in the shape of the stroma

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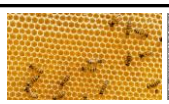
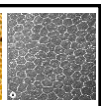
# Endothelium

141

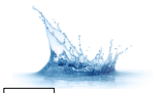
## Endothelium

A **single layer** of cells that **covers the posterior cornea** in a well-arranged mosaic pattern





The Endothelium's Job Description




Pump

Pump

Pump

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## Endothelium's Leaky "Problem"

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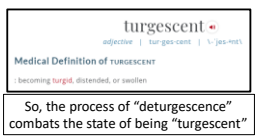
## Deturgescence

The physiological process in which the stroma of the cornea is kept relatively "***dehydrated***" to maintain normal corneal clarity and transparency




So, the process of "deturgescence" combats the state of being "turgescent"

The **cornea** strives to be **78% water**

***turgid***: swollen ***turbid***: opaque

Therefore,
a **turgid** (***swollen***) cornea leads to a **turbid** (***opaque***) cornea

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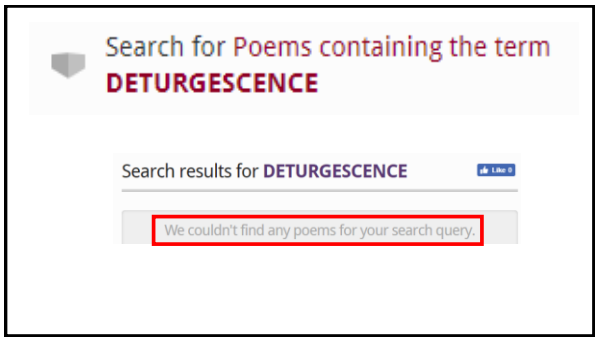


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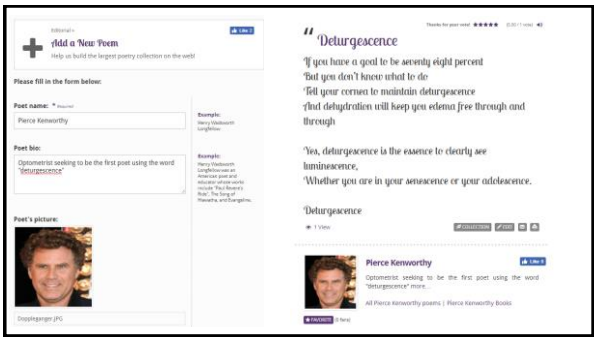


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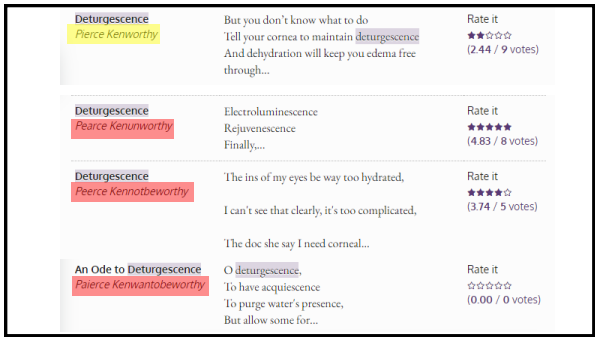


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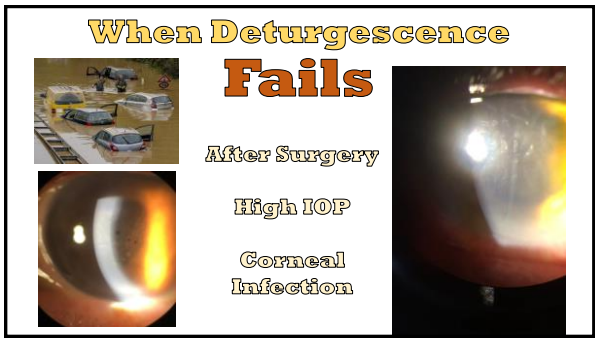


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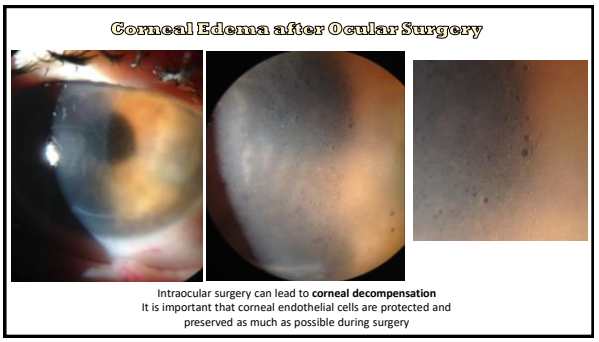


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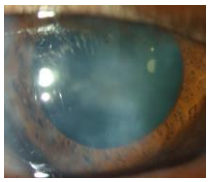
## High Intraocular Pressure

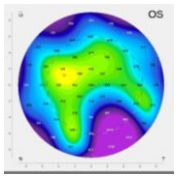
- The level of intraocular pressure (IOP) can have a profound and variable effect on corneal stromal hydration
  - **Chronic high pressure** leads to **endothelial damage** and subsequent **edema**
- In the setting of either acute or insidious (*gradual*) IOP elevation, decreasing the pressure can improve or resolve corneal edema and prevent further damage to endothelial cells


151

## Corneal Infection/Inflammation

**Ex. Herpes Simplex Disciform Keratitis**
Recurrent corneal infection and inflammation






Endotheliitis causing corneal edema

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## 3 Important Characteristics of Endothelium

**Density** (should be high)

**Size** (should be small and consistent)

**Shape** (should be hexagonal)

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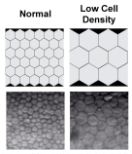
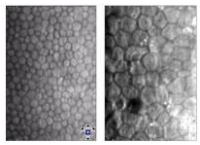
## Density (should be high)

- ***Cell density (CD) is a measurement of cell density in mm²***
- As these cells ***do not have the ability to replicate***, humans are born with the maximum number of endothelial cells they will ever have
- **Endothelial cell density decreases with age and disease**
  - Kids cell density ~4000 cells/mm²
  - Young adults cell density ~3500 cells/mm²
  - By age 80 years, cell density ~1000-2000 cells/mm²



Normal Endothelium High Cell Density

Very Low Density

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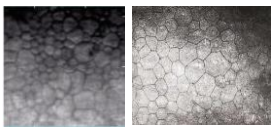
## Size (should be small and consistent)

- The **coefficient of variation** (***standard deviation/mean***) for cell area is a clinically valuable marker as it represents ***degree of variation in size***
  - ***On average***, it is about **25% in the normal cornea**
- An **increase in the variability of cell area** is termed **polymegathism** (**variation in cell size**)



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## Polymegathism in the real world??

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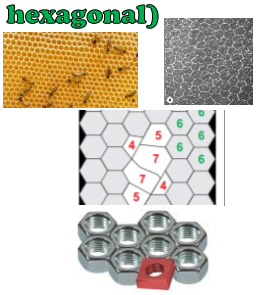
# Shape (should be hexagonal)

- **Normally are hexagonal** (***but can have 5 to 7 sides at times***)
- **Deviation from hexagonality** is referred to as **pleomorphism**
- In the **normal** healthy cornea, on ***average*** **70–80%** of endothelial cells are **hexagonal**
- **Endothelial damage** can result in a decrease in the hexagonality value

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# Specular Microscopy

The endothelial cell **density**, **size** and **shape** can be evaluated by specular microscope

***CD = cell density***

***CV = coefficient of variation*** ***represents the degree of variation in the sizes of the endothelial cells***

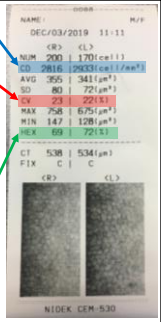
CV less than 40 being normal

***Measure of polymegathism***

***HEX = indicates the variability in hexagonal cell shape over time***

Hexagonality above 50% is suggested to be normal

***Measure for pleomorphism***

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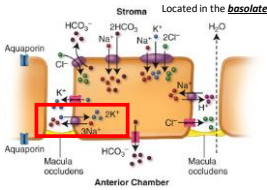
# Na/K ATPase

A major transport protein found to be essential for endothelial metabolic pump function is **Na+ /K+ -ATPase**

Located in the ***basolateral membrane*** *of endothelial cells*




***enzyme transports 3 Na⁺ ions out in exchange for 2 K⁺ ions that are taken into the cell***

Studies have shown that approximately **3 million Na+ /K+ -ATPase pump sites** are present in the basolateral membrane of a **single corneal endothelial cell**

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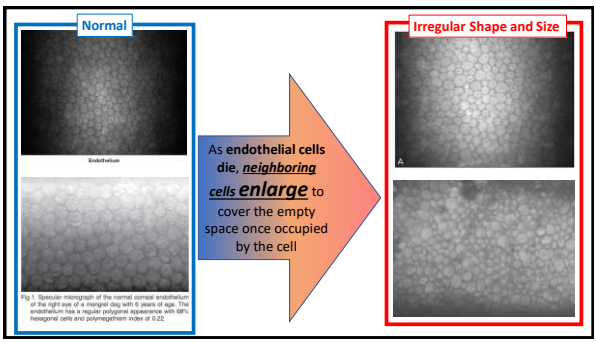


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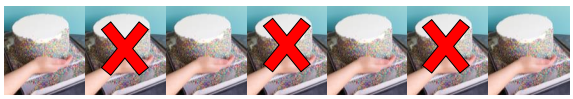
If those sprinkles are ***actually*** NaK pumps on the basolateral membrane, then which layer will more effectively pump fluid?



Healthy endothelial cell density (tall with sufficient room on basolateral sides for pumps)

Low endothelial cell density (cells are flattening and spreading, less room for pumps)

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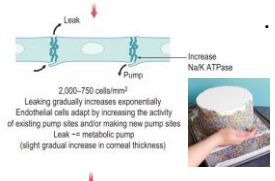


- Between **2000 and 750 cells/mm2, compensatory** metabolic pump mechanisms help prevent corneal edema
  - **The total number and density of pump sites on the lateral membranes of endothelial cells increases**
  - **The metabolic activity of pump sites already present increases**

- When the central endothelial cell density (ECD) reaches approximately **500 cells/mm2 or less, compensatory** mechanisms ultimately ***fail***
  - Endothelial cells are **spread so thin** that they do **not** have enough room on their lateral cell membranes for more metabolic pump sites
  - All the existing pump sites are maximally active

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## Clinical Comment:

# Fuchs Endothelial Corneal Dystrophy

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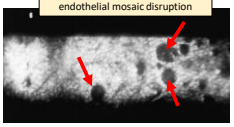
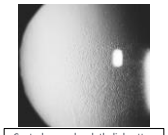
## Fuch's Endothelial Dystrophy

In Fuchs' endothelial dystrophy, the cornea has focal areas of very low endothelial cell density

In early stages of Fuch's, **initially** the cornea may remain clear and of normal thickness because of **compensatory mechanisms**

With ***more advanced Fuch's***, endothelial **decompensation** leads to stromal edema

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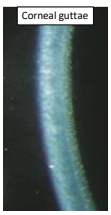
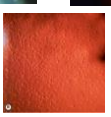
## Stage 1

- In Stage 1, the initial manifestation of the disease is central **corneal guttae** (plural for guttata).
- Many patients at this early stage are not symptomatic
  - However, some patients do complain of **glare** and a **decreased quality of vision**
- Some patients remain at Stage 1 and never progress further.

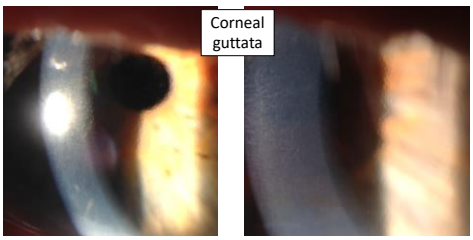






165

## 2016 - 74 yo female, pseudophakic patient, experiencing ***glare*** at night

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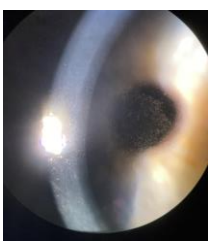
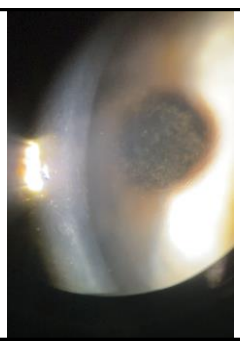
## 2023-07-28, 76 yo female, what's that finding in the right eye





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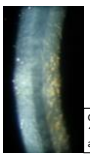
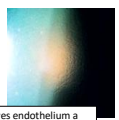
## Stage 2

- Stage 2 is characterized by **endothelial decompensation and stromal edema**
- In this stage the **guttae have spread peripherally and may coalesce**, producing a ***beaten metal appearance***
  - May present with or without pigment dusting.
- The **Descemet membrane becomes visibly thickened**, gray, and irregular
- Progressive stromal edema results in a ground glass opacification of the cornea with marked central thickening.
- At this point in the disease, the ***patient's vision will be reduced, most prominently in the morning***

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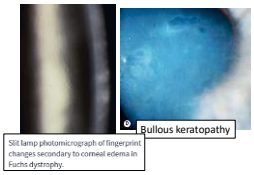
## Stage 3

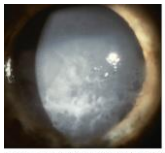
- Stage 3 is marked by **bullous keratopathy**
- The irregularity of the corneal surface and stromal haze further reduce vision




Slit lamp photomicrograph of fingerprint changes secondary to corneal edema in Fuchs dystrophy.

## Stage 4

- Stage 4, end stage disease, is characterized by **avascular subepithelial fibrosis and scarring** between the epithelium and Bowman's membrane



Slit lamp micrograph of subepithelial fibrosis and bullae in Fuchs dystrophy.

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## Fuchs Endothelial Corneal Dystrophy Management

Patients with **early FECD** may be asymptomatic and require no treatment

Currently, there is **no medication** that will prevent the progression of Fuchs

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## Fuchs Endothelial Corneal Dystrophy Management

- With progression of FECD, patients may ***complain of decreased vision on awakening***, from the **accumulation of fluid in the cornea while sleeping**
  - With slight stromal edema, the vision may spontaneously improve after a short time of eye opening as the air facilitates evaporation of stromal fluid
- This type of patient may achieve **temporary relief** by use of **hypertonic saline solutions or dehydration** of the cornea by a fan or blow dryer
  - These approaches temporarily dehydrate the cornea and improve vision
- **If the patient achieves no relief by these approaches, there is no reason to continue them** as they are only symptomatic and **do not change the course of the disease**


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## Hair dryer will be just fine

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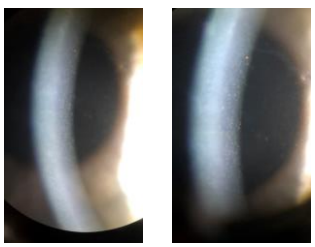
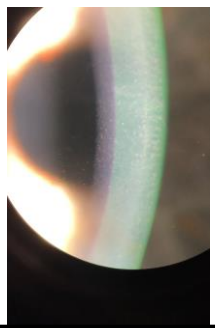
2021-08-11, 73 yo female, was told she "had some problems with cornea" by another doctor and "***might eventually need a graft***"





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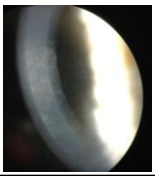
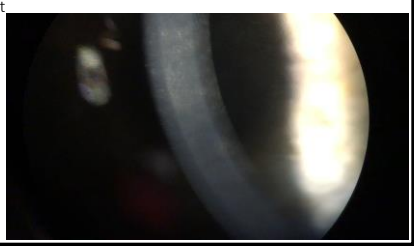
76 yo female, **1 week cataract post-op OS**

Pt w/ Fuch's, had cataract surgery and now only seeing **20/60 OS**

**"Why am I not seeing well after cataract surgery??"**





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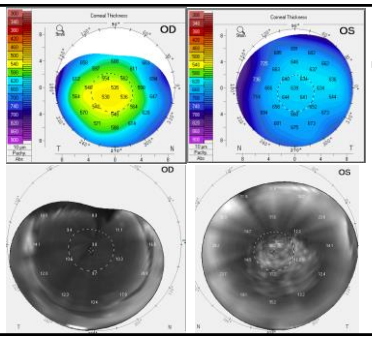
OD had an endothelial transplant (DMEK)




Notice how much **thicker OS** cornea is (did NOT have a DMEK – **still has Fuch's**)

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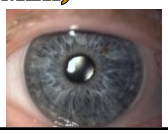
# Endothelial Keratoplasty

## Descemet's Stripping Automated Endothelial Keratoplasty (DSAEK)

## Descemet Membrane Endothelial Keratoplasty (DMEK)

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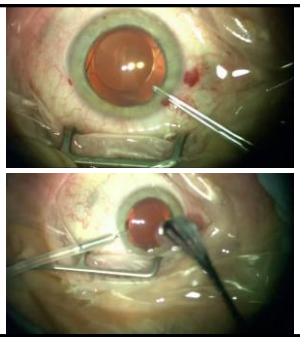
## Fuchs Endothelial Corneal Dystrophy **Surgical** Management

- **Descemet stripping automated endothelial keratoplasty (DSAEK)** has become the mainstay of surgical treatment for visually significant FECD – Fuch's Endothelial Corneal Dystrophy (mostly replacing PKP)
- According to Eye Bank statistical report, endothelial dystrophies (including FECD) were the most common indication (48.6%) for DSAEK
  - The next largest group (19.1%) was for **post-cataract surgery edema**
- DSAEK
  - Descemet membrane stripping automated endothelial keratoplasty
- DMEK
  - Descemet membrane endothelial keratoplasty



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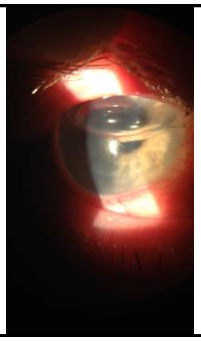
1 day post DSAEK

Anterior chamber air bubble



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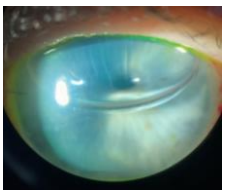
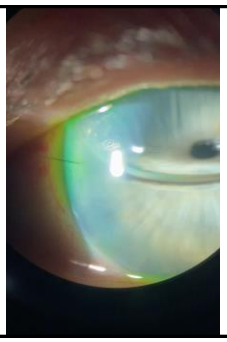
2023-07-28, 76 yo female, one day post DMEK





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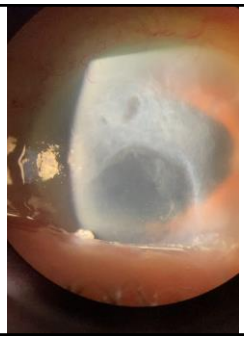
## Emergency Call from Concerned Patient on Saturday

- Had "corneal graft" and "cataract surgery" on Tuesday
- Woke up today and noticed horizontal line across eye and achy pain

180

2023-09-01, 81 yo female, OS hx of pseudophakic bullous keratopathy (HM)



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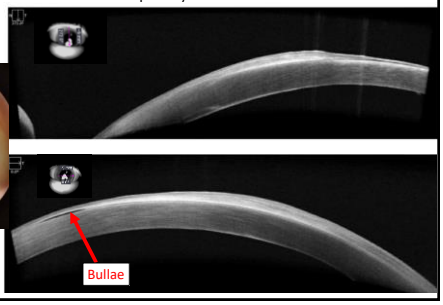
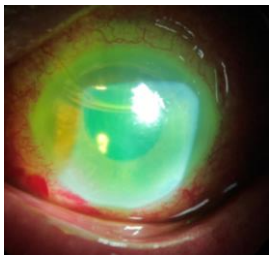
OS pseudophakic bullous keratopathy





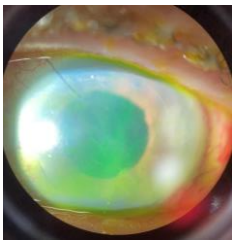

182

2023-09-15, OS one day post DSAEK



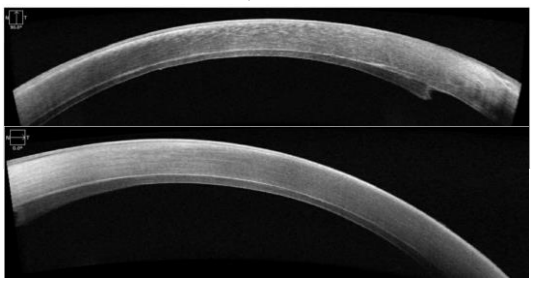
183

2023-09-22, OS one week post DSAEK



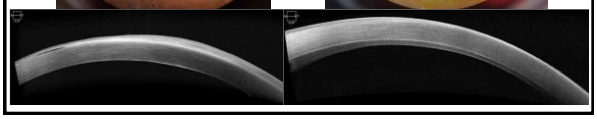
184

2023-09-27, two week post DSAEK



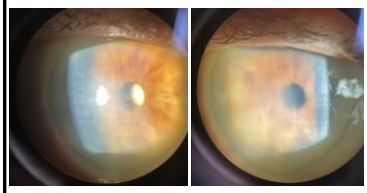
185





186

2023-10-20, 90 yo male, 2.5 week post DMEK for Fuch's dystrophy. VA CF right eye. What do you think of post op appearance?



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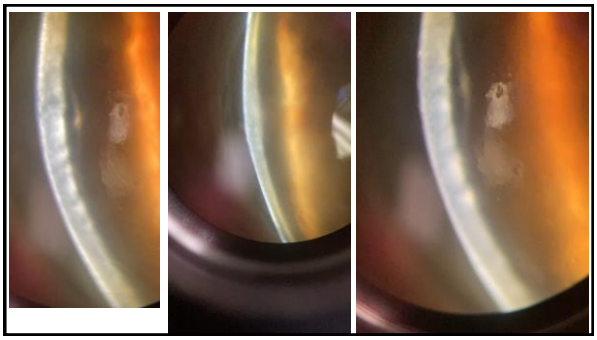

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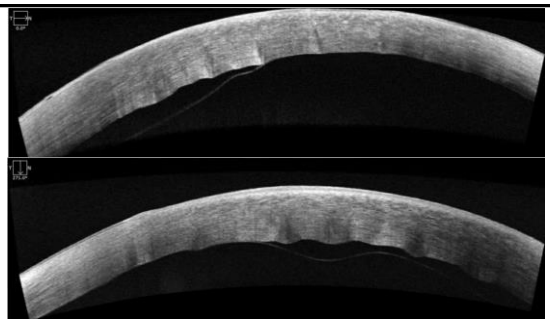
189



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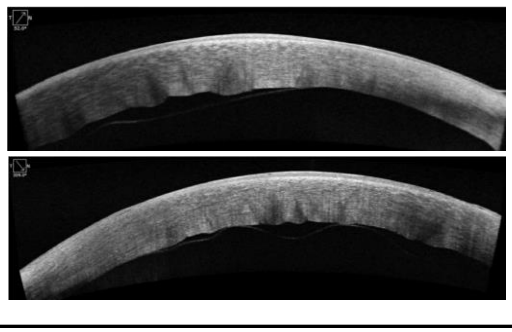
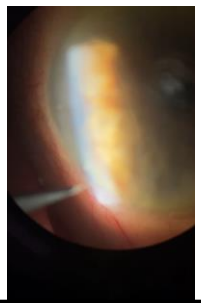
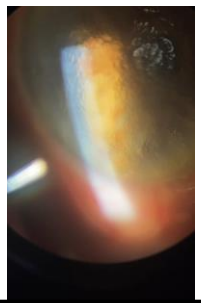


191

I'm coming in!



Bring on the air



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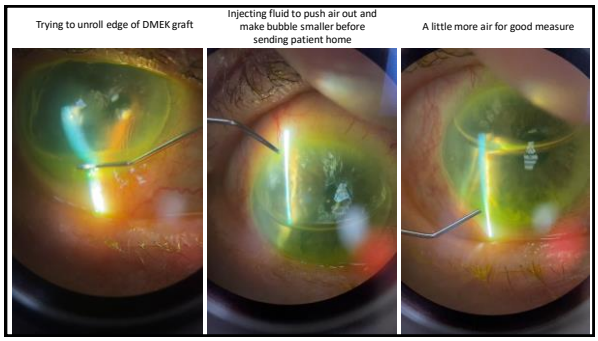


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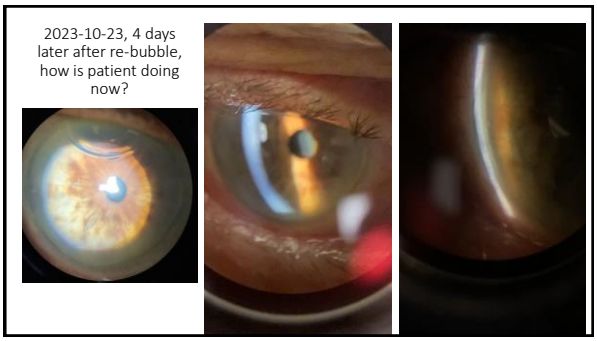


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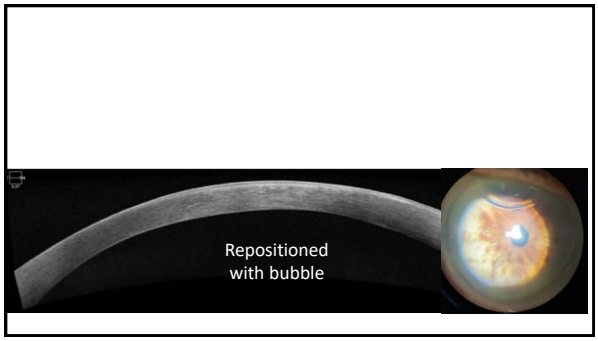


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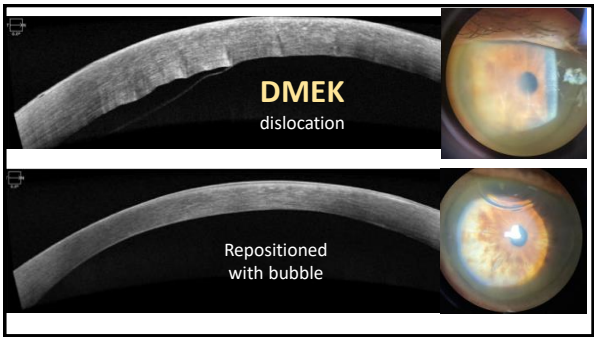


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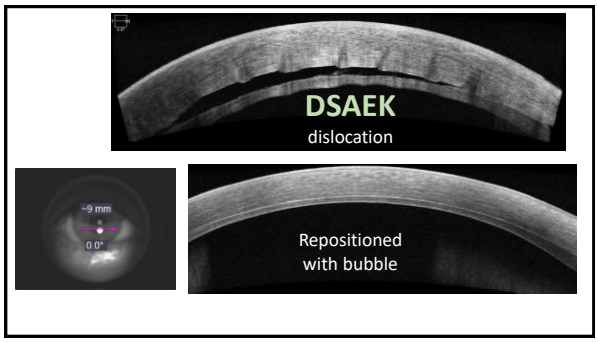


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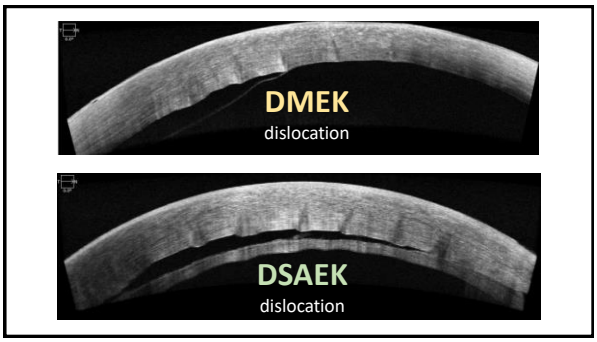



198

# What happens if you remove corneal endothelium but don't replace it with anything?

**Descemet's Stripping Only (DSO)**
**[aka. Descemetorhexis without endothelial keratoplasty (DWEK)]**

199

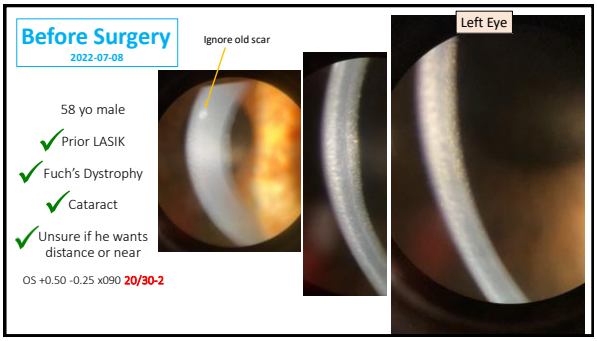
# DSO
## Descemet's Stripping Only

## [aka. DWEK
## Descemetorhexis *without* endothelial keratoplasty]

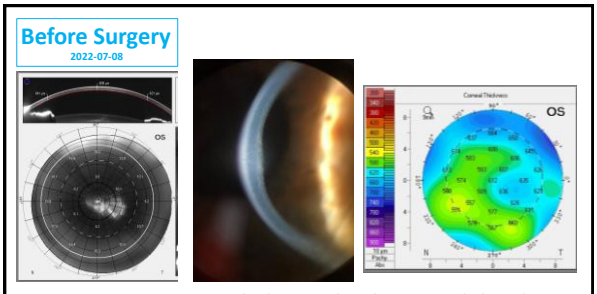
200

# DSO/DWEK Example #1

201




202

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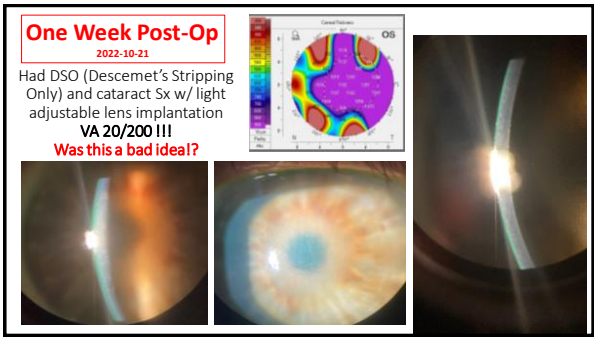


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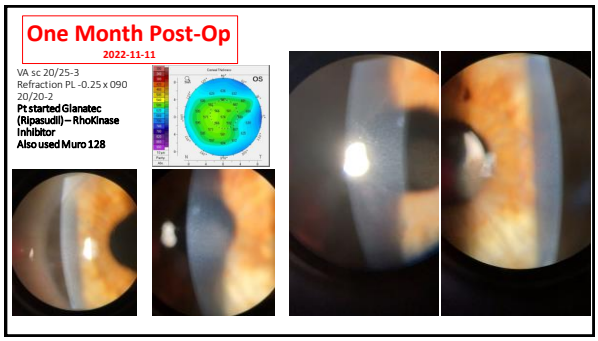


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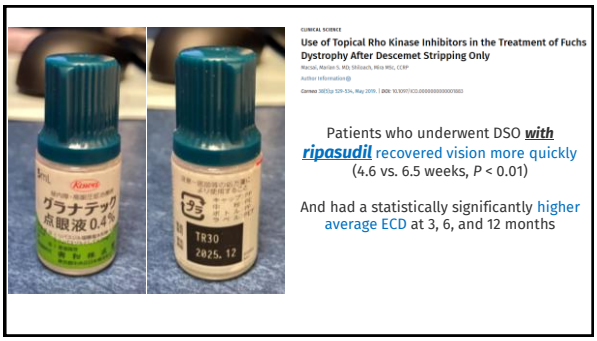
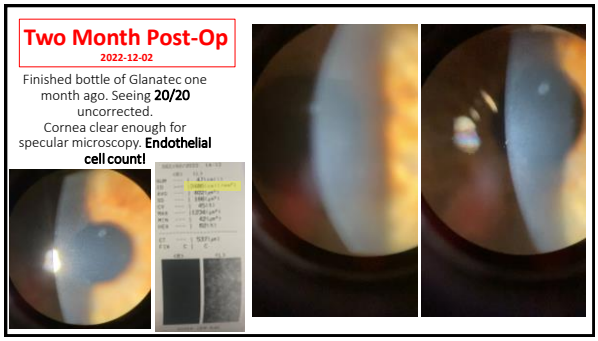



206

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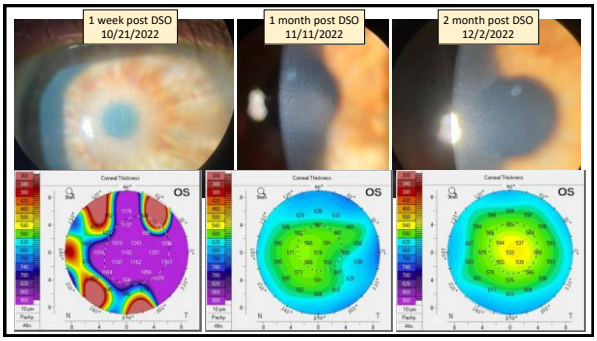


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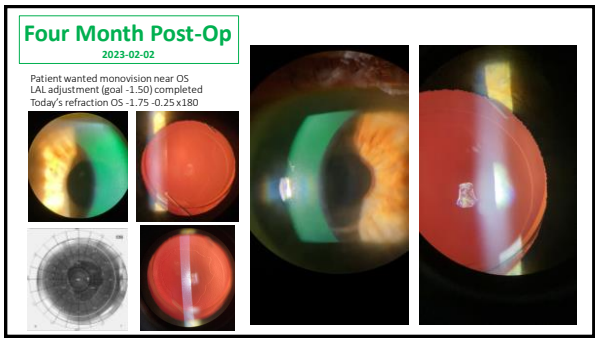


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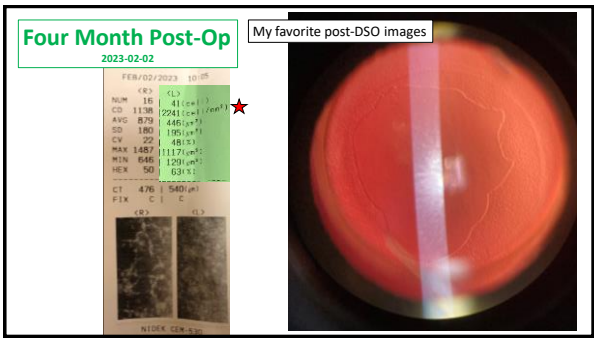


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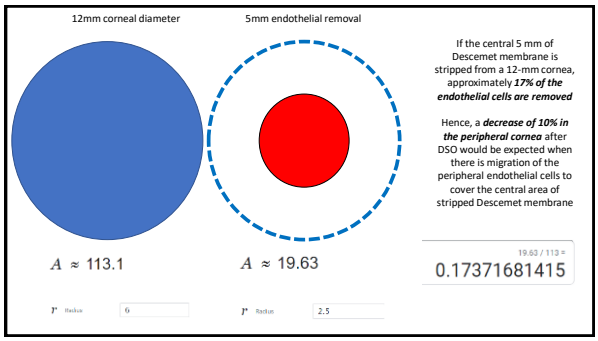



211


212

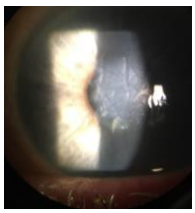
213

# DSO/DWEK Example #2

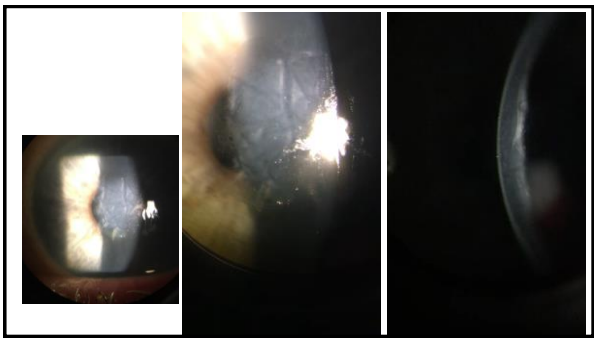
214

62 yo female, OS combo cataract and **DWEK (Descemetorhexis Without Endothelial Keratoplasty) [aka DSO]** 3 weeks ago.

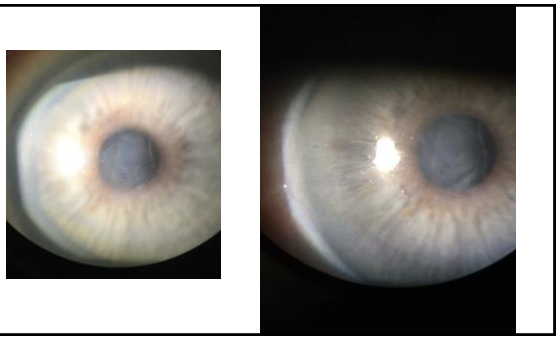
Why is the central cornea so cloudy!? She has NO endothelium in center



215

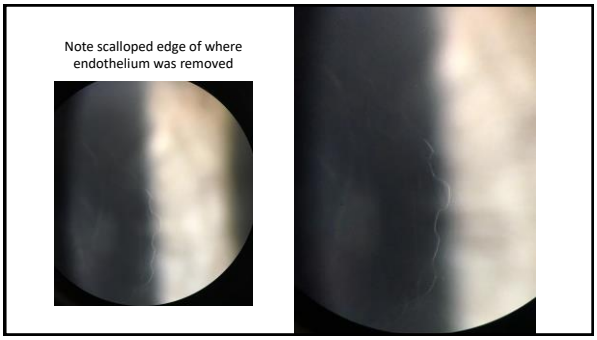


216



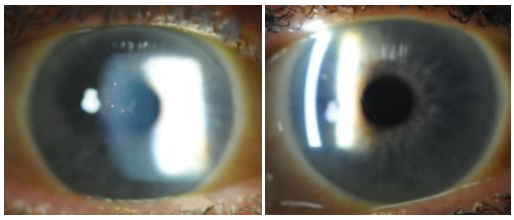
217

Note scalloped edge of where endothelium was removed



218

August 2020 (one year follow up)



Right Eye
Cataract Surgery only

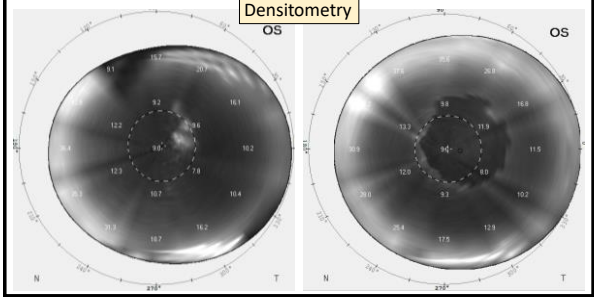
Left Eye
Cataract Surgery **and DWEK**

219

Before DWEK

Densitometry

One year after DWEK

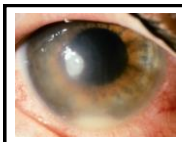



220

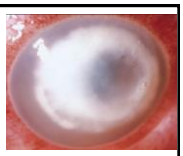
# Contact Catastrophes

221

# Bacterial Keratitis



Pseudomonas keratitis associated with extended wear soft contact lens. A paracentral corneal infiltrate with surrounding corneal edema and hypopyon.



A ring of necrotic stromal infiltrate in a Pseudomonas keratitis, simulating Acanthamoeba keratitis

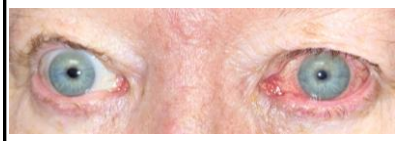
**Contact lens wear** has been identified as the **most common risk factor** for bacterial keratitis in developed countries

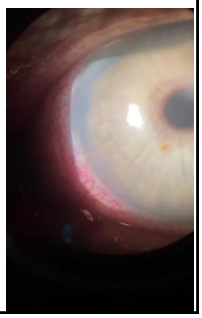
***Pseudomonas* spp. are the most common contact lens-associated pathogen in bacterial keratitis**

**Continuous lens wear increases the risk of infectious keratitis by approximately 10-fold**

222

2023-12-08, 64 yo female, red, painful (6/10) OS that started two days ago. Used old prednisolone and diclofenac gtts OS and states that it helped a little. Pt is not currently a contact lens wearer (***states she has NOT worn a contact in over a year).*** Vision is foggy, like seeing through a dirty window (VA 20/200)





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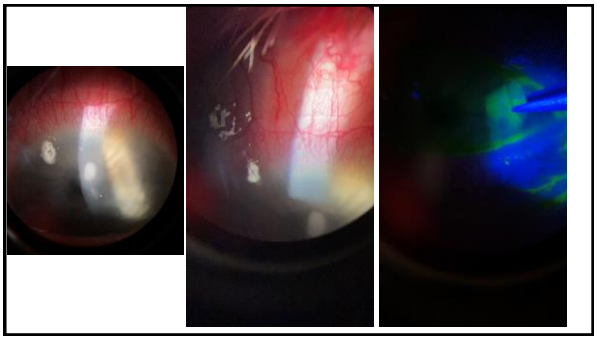

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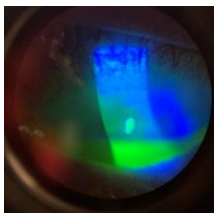

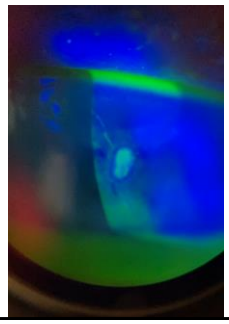

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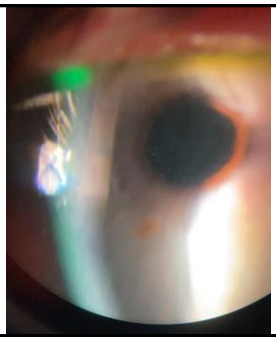
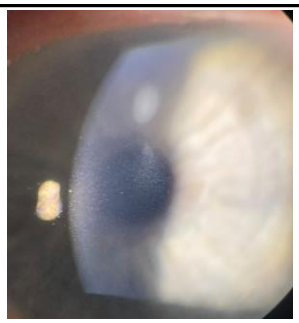


226

2023-12-22, one week follow up after resolution with moxifloxacin



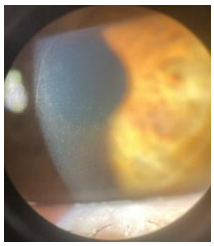
227

24 yo male, had a great birthday party last night with some cold ones, became inebriated and slept in contact lenses. Woke up with…

Corneal culture results were positive for **pseudomonas**. Was treated successfully with ***topical moxifloxacin***

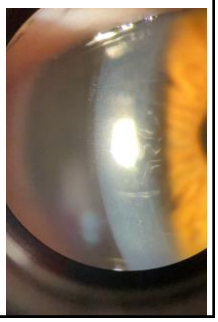
228

61 yo female, OD still feels dry. Didn't like side effects from Xiidra. Had inferior puncta cauterized. Wants to "fix" her cornea.




229

1 week f/u, returned for BCL removal (7 days total). Pt said a couple days eye started bothering her and got red



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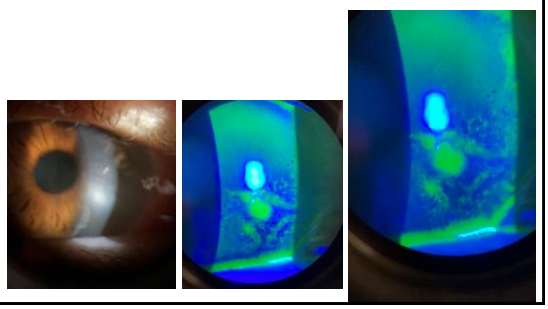
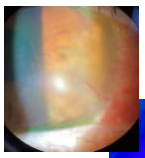
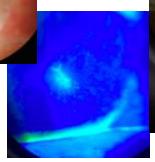
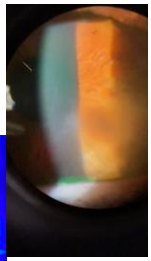


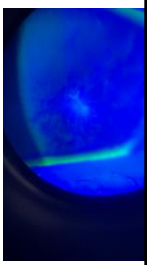
231

1 day ulcer follow up – taking moxifloxacin q1hr
Is it getting better or worse?







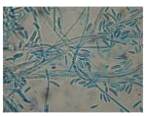


232

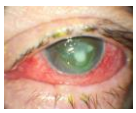
# Keratitis

## Confocal Microscopy

233



# Fungal Keratitis



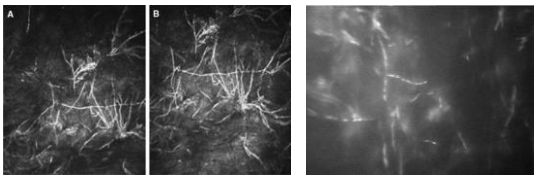
The most common organisms isolated in fungal infections include **Candida, Aspergillus, and Fusarium**

**Trauma with vegetable-contaminated matter** is a major risk for **fungal keratitis**

**Soft contact lenses** are becoming a more common cause

234

## Confocal Microscopy of Fungal Keratitis

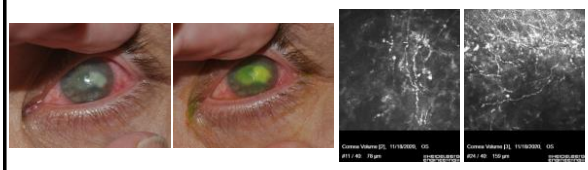



Hyper-reflective linear structures with acute angle branching, typical of fungal hyphae

Hyper-reflective, branched, septated, linear structures suggestive of fungal structures

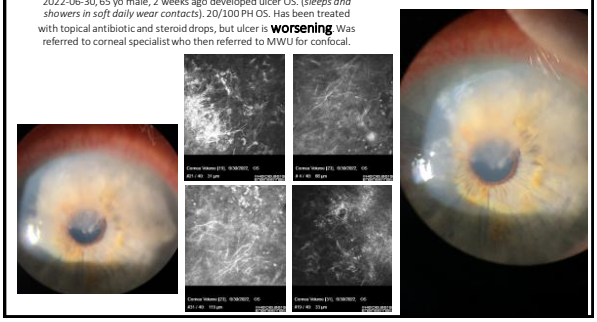
235

2020-11-18, 55 yo male referred for second opinion on non-resolving corneal problem. Pt has **slept in contacts for 40+ years**. Recently used hot tub while wearing contacts, also visited Mexico where house had untreated water. Showers and swims in his contact lenses



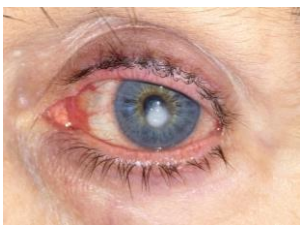
236

2022-06-30, 65 yo male, 2 weeks ago developed ulcer OS. (*sleeps and showers in soft daily wear contacts*). 20/100 PH OS. Has been treated with topical antibiotic and steroid drops, but ulcer is **worsening**. Was referred to corneal specialist who then referred to MWU for confocal.

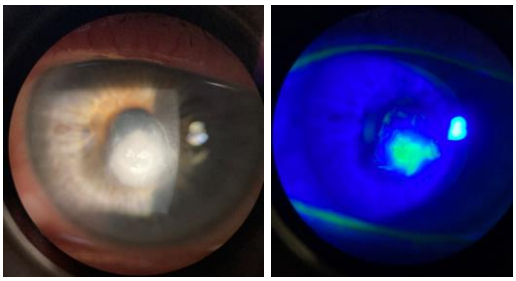


237

2023-12-08, 67 yo female, hx of corneal ulcer OS x 3 months. Is down to steroid about once or twice a day (stings upon instillation). Pt is also using Valtrex 1gram qd. Using vancomycin and tobramycin alternating every hour. Pt reports light sensitivity. Also has occasional stabbing pain with 8 out of 10 pain. Vision poor, with minimal change/improvement. Pt has hx of CL use from 6am to 3pm. Referred for confocal

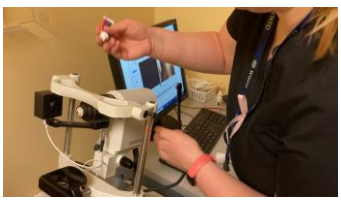


238

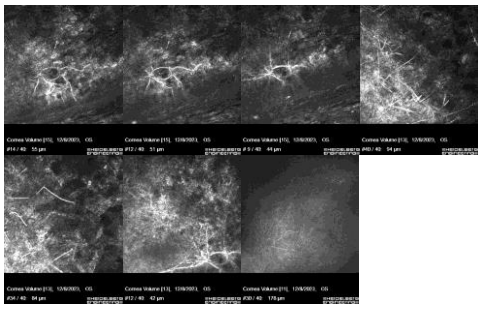


239

## Confocal

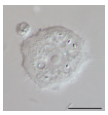


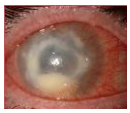
240



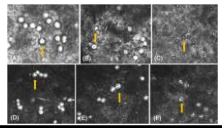
241

# Acanthamoeba Keratitis

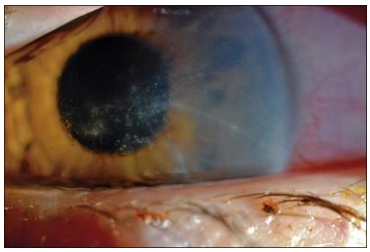




Acanthamoeba are ubiquitous **protozoa** (*protozoa* = single celled organism that feeds on organic material) found in soil and fresh water. The majority of reported cases of **acanthamoeba keratitis** in Western countries have been associated with **contact lens use**.



242



**Epithelial keratitis and radial keratoneuritis due to Acanthamoeba infection**

*(can see enlarged corneal nerves)*

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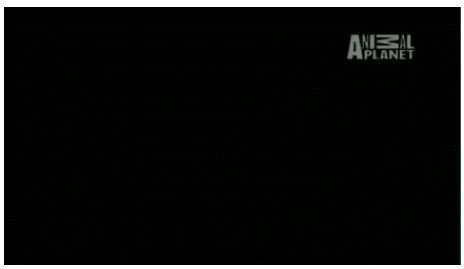
**Mom temporarily blinded by parasite after swimming with contacts**

**Woman claims she lost eye after parasite got stuck behind contact lens during shower**

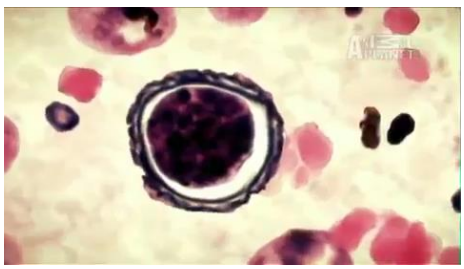
244

Gloom and Doom???




245

Gloom and Doom???



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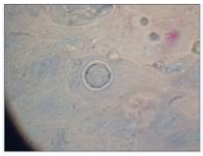
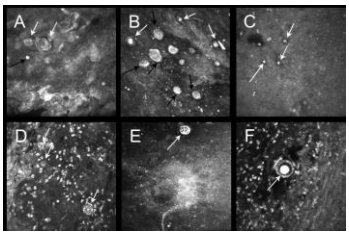
## Double walled cysts of Acanthamoeba may be visualized with confocal microscopy

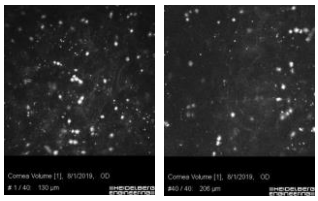


*Acanthamoeba* cyst from a superficial corneal scraping. (Diff-Quik Stain,




247

34-year-old Caucasian male was referred for a second opinion due to suspected microbial keratitis after falling into a lake with his soft contact lenses. He then slept in his contact lenses for several nights
Symptoms began approximately 2 weeks after. First went to urgent care who diagnosed corneal abrasion…



Acanthamoeba visualized with confocal microscopy

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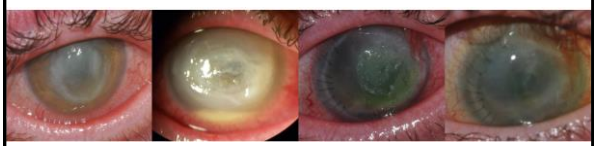
## Utilizing Confocal Microscopy

Florencia Yeh OD, FAAO, FSLS and Robert E. Fintelmann, MD, FACS
Midwestern University Arizona College of Optometry, Glendale, AZ



**Day 84**
ring infiltrate

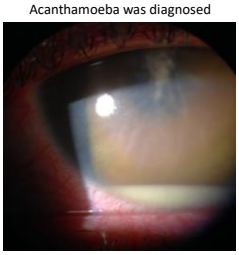
**Day 161**
corneal melt

**Day 377**
non-resolving epithelial defect

**Day 476**
Glue patch over area of thinning

249

24 year old male, was swimming in Lake Havasu with contacts and developed eye infection about 2 months ago.
Acanthamoeba was diagnosed

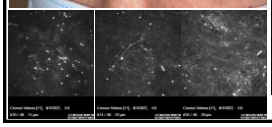


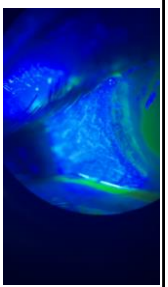
250

2022-08-03, 42 yo female presents with red, painful eye OS.

Three weeks ago, **urgent care** diagnosed her with a **corneal abrasion OS** and gave **her "antibiotic drops".**
Symptoms didn't improve so pt went to **OD who suspected bacterial keratitis and put her on Ofloxacin gtts**
Days later still not improving so OD **referred her to large OD/MD group, and they switched her to a steroid**. Symptoms started to get "very bad."

"worst pain I've ever experienced" (History of sleeping and swimming in contact lenses)





251

2022-05-17, 45 yo male. Hx of acanthamoeba in January 2022. Had a therapeutic PKP in March because cornea became necrotic. Graft is failing. Back for confocal to rule out acanthamoeba.

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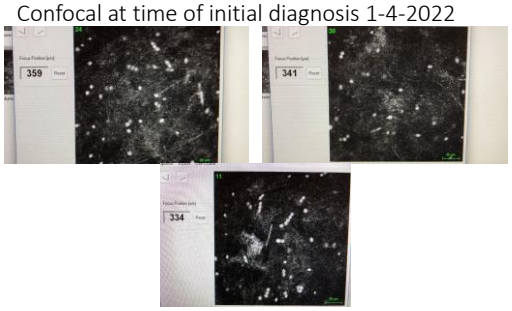
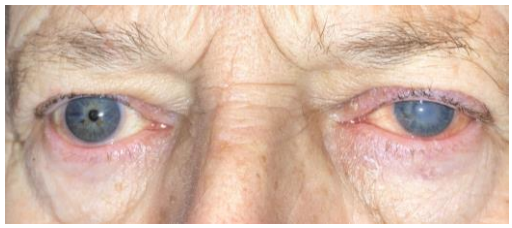
Confocal at time of initial diagnosis 1-4-2022

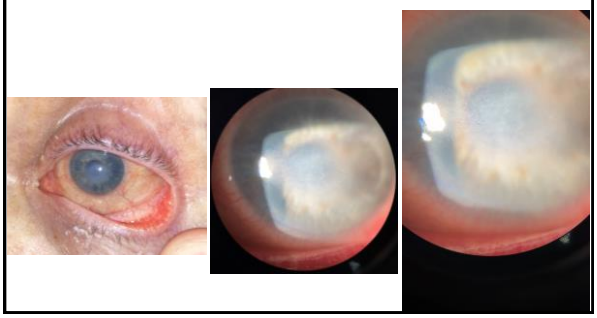



253

2023-11-15, 69 yo male, hx of acanthamoeba diagnosed 6 months. Just stopped chlorhexidine and PHMB two weeks ago. Eye feels so much better now that he stopped drops.



254



255

Just Wear Glasses!

**Protect the Cornea**

**The Cornea's Best Friend**

Thank you for your time

pkenwo@midwestern.edu

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