Advanced treatments of chronic corneal disease

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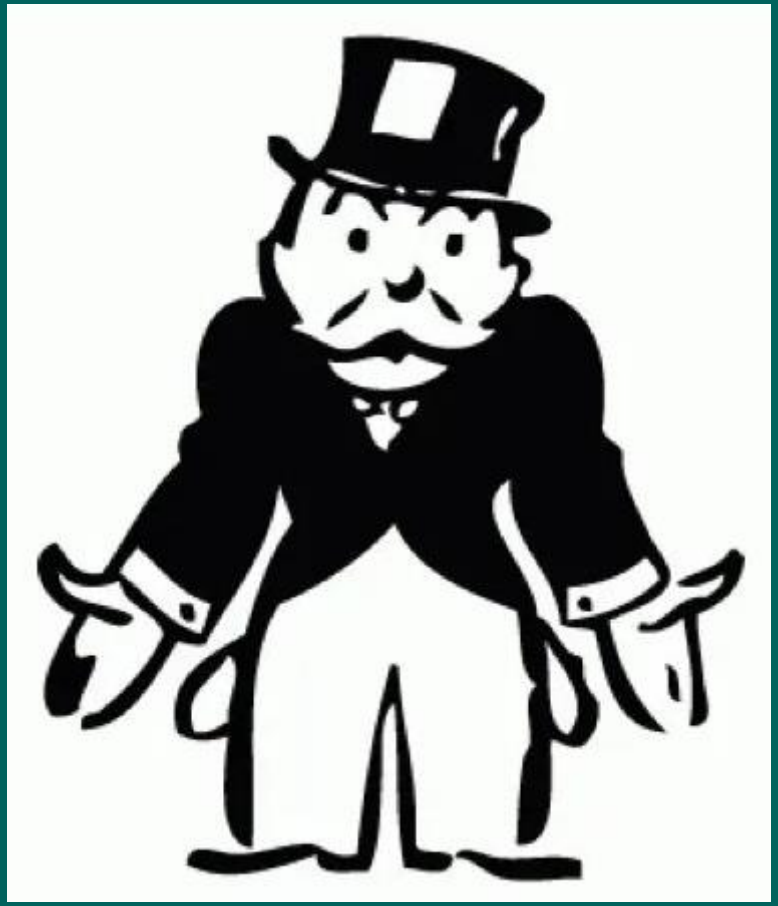
I have no financial conflicts or disclosures.



Objectives

- Two cases involving chronic corneal disease
- Review of corneal topography interpretation
- Various treatment strategies
- Systemic effects of supplements and medications

Case 1 Visit 1 History

- 27 y/o WM presents for his first eye exam
- cc: blurred vision when driving gradually getting worse over the last few months
- No systemic medication
- Medical history unremarkable
- Family history unremarkable

Case 1
Visit 1
Pre-testing

- UCVA: OD 20/40 | OS 20/30
- Pupils: ERRL D&C –APD
- Confrontation VF – FTFC OD and OS
- Color vision: 10/10 Ishihara
- CT: ortho at distance
- EOMs: SAFE

Case 1
Visit 1
Refraction

- Auto refraction
  - OD +0.50 -5.25 x 052
  - OS +0.50 -3.50 x 145
- Auto keratometry
  - OD 43.50 @ 052 | 49.25 @ 142
  - OS 43.00 @ 144 | 46.50 @ 054
- Refraction
  - OD +0.50 -2.50 x 050 | 20/25-2
  - OS +0.50 -1.00 x 145 | 20/20

Case 1
Visit 1
SLE/fundus OU

- Lids/Lashes: clear
- Conjunctiva/sclera: white and quiet
- Tear film: clear
- Cornea: clear
- AC: deep and quiet
- Iris: flat
- Lens: clear
- Vitreous: clear
- ONH: clear margins; 0.30 H/V
- Posterior pole: clear
- Peripheral retina: flat and attached

Case 1
Visit 1
Assessment/Plan

- Mixed astigmatism OD>OS w/ refractive amblyopia OD
- Rx glasses – pt ed on adaptation to new rx – f/u in 6 weeks for amblyopia check/adaptation to new rx

Case 1 Visit 2 History

- Six weeks after visit 1
- cc: pt says his vision is better compared to not wearing glasses, but his vision on the right is still blurry compared to his left

Case 1
Visit 2
Rx check

- VA cc: 20/30- OD | 20/30 OS
- Auto refraction
  - OD -2.00 -4.75 x 044
  - OS -0.75 -2.00 x 138
- Auto keratometry
  - OD 43.75 @ 052 | 49.25 @ 142
  - OS 43.00 @ 143 | 46.50 @ 053
- Refraction
  - OD: plano -3.00 x 050 | 20/25-
  - OS: plano -1.25 x 145 | 20/20-

Case 1
Visit 2
Assessment/Plan

- No improvement in amblyopia
- Refer for VT consultation

Case 1
Visit 3
Same practice different doctor

- Had not had VT eval scheduled, but feels his vision is getting blurrier when using his computer.
- “Letters have shadows”
- Refraction was updated with Eyezen to improve computer vision.
- Reiterated need for VT evaluation
- Otherwise, monitor 1 year


ONE YEAR
LATER...

Case 1
Visit 4
Comprehensive Exam

- Patient never had VT consultation
- Medical history stable
- Feels vision is getting gradually worse, especially at the computer
- VA at distance cc: OD and OS 20/40
- VA at near cc: OD and OS J2

Case 1
Visit 4
Comprehensive Exam

- Auto refraction
  - OD -2.00 -6.00 x 051
  - OS -1.50 -2.75 x 140
- Auto keratometry
  - OD **no reading**
  - OS 43.50 @ 143 | 48.50 @ 053
- Refraction
  - OD: +0.75 -2.50 x 056 | 20/25-
  - OS: plano -1.25 x 125 | 20/20-

Case 1
Visit 4
Assessment/Plan

- Maintained diagnosis of refractive error with amblyopia OD and accommodative dysfunction
- Update glasses to PALs to improve computer vision
- Reiterated the importance of VT consultation

Case 1 Consultation

- Patient referred for “specialty lens fit” because not fully correctable with glasses.
- Glare very bothersome. Letters have shadows on his computer OD>OS
- VA cc
  - OD 20/25-
  - OS 20/20-

ZEISS

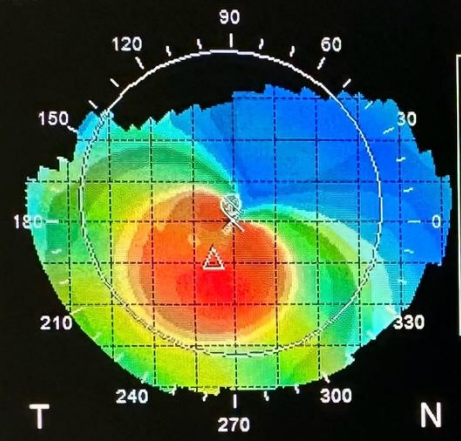
Family Eye Care of Apex

OD/OS Compare

Axial Curvature OD

Standard palette
Auto scale

66.0
63.0
60.0
57.0
54.0
51.0
48.0
45.0
42.0
39.0
36.0
33.0
1.5 D

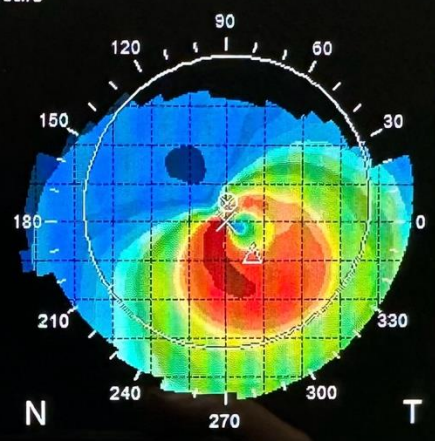


Steep K	52.71 D @ 132
Flat K	47.10 D @ 42
Astigmatism	5.61 D
Eccentricity	0.72
Q	-0.52
Shape Factor	0.52
Pup. diam	7.3 mm
HVID	12.8 mm

Axial Curvature OS

Standard palette
Auto scale

59
57
55
53
51
49
47
45
43
41
39
37
1 D



Steep K	49.48 D @ 65
Flat K	46.15 D @ 155
Astigmatism	3.33 D
Eccentricity	0.89
Q	-0.79
Shape Factor	0.79
Pup. diam	7.5 mm
HVID	12.9 mm

Keratometry OD

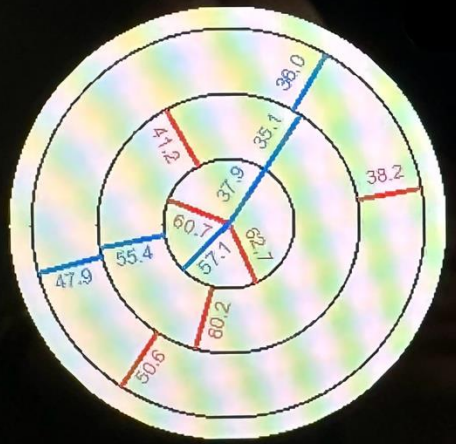
Sim Ks (3 mm)
52.71 D (6.40 mm) @ 132
47.10 D (7.17 mm) @ 42

Total astigmatism 5.61 D

Central (0-3 mm)
62.74 D (5.38 mm) @ 294
60.70 D (5.56 mm) @ 158
37.87 D (8.91 mm) @ 56
57.12 D (5.91 mm) @ 224

Midperiphery (3-6 mm)
60.20 D (5.61 mm) @ 254
41.21 D (8.19 mm) @ 118
35.08 D (9.62 mm) @ 56
55.37 D (6.10 mm) @ 190

Periphery (6-9 mm)
50.63 D (6.67 mm) @ 236
38.24 D (8.83 mm) @ 10
36.00 D (9.38 mm) @ 60
47.86 D (7.05 mm) @ 194



Keratometry OS

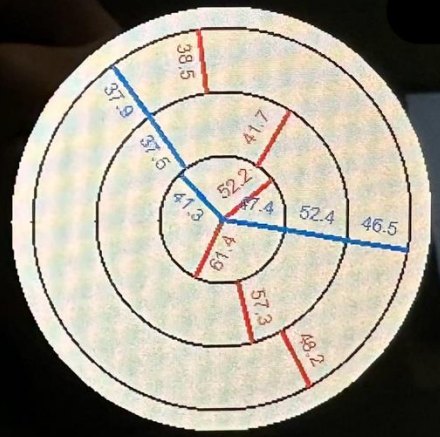
Sim Ks (3 mm)
49.48 D (6.82 mm) @ 65
46.15 D (7.31 mm) @ 155

Total astigmatism 3.33 D

Central (0-3 mm)
61.37 D (5.50 mm) @ 244
52.17 D (6.47 mm) @ 38
41.33 D (8.17 mm) @ 132
47.44 D (7.11 mm) @ 350

Midperiphery (3-6 mm)
57.28 D (5.89 mm) @ 284
41.74 D (8.09 mm) @ 58
37.46 D (9.01 mm) @ 126
52.39 D (6.44 mm) @ 350

Periphery (6-9 mm)
48.15 D (7.01 mm) @ 298
38.54 D (8.76 mm) @ 98
37.86 D (8.91 mm) @ 126
46.45 D (7.27 mm) @ 350



 ATLAS Revision 3.0.0.39

Case 1 Diagnosis and plan

- Keratoconus OU
- Fit with ZenLens (Bausch and Lomb) scleral contact lenses

Case 1
CL summary

- Successful I&R
- Three visits with adjustments to sagittal height and powers from initial fitting
- VA cCL
  - OD 20/15
  - OS 20/15
- Discussed corneal cross-linking
- Monitor 6 months CLCK

Case 1
1 year later

- The 6-month check was uneventful.
- He has no complaints and wears the lenses 14+ hours/day.
- Refraction
  - OD pl -3.00 x 090 | 20/40
  - OS -1.00 -2.00 x 135 | 20/40
- Topography – poor readings
- SLE cornea OU: no stria noted, slight epithelial haze centrally

Case 1
1 year later
CL eval and plan

- Still good scleral alignment
- VA cCL
  - OD 20/20
  - OS 20/20
- Minimal to no central clearance
- Ordered new lenses with increased sagittal height and adjusted power

Case 1
1 year later
CL eval

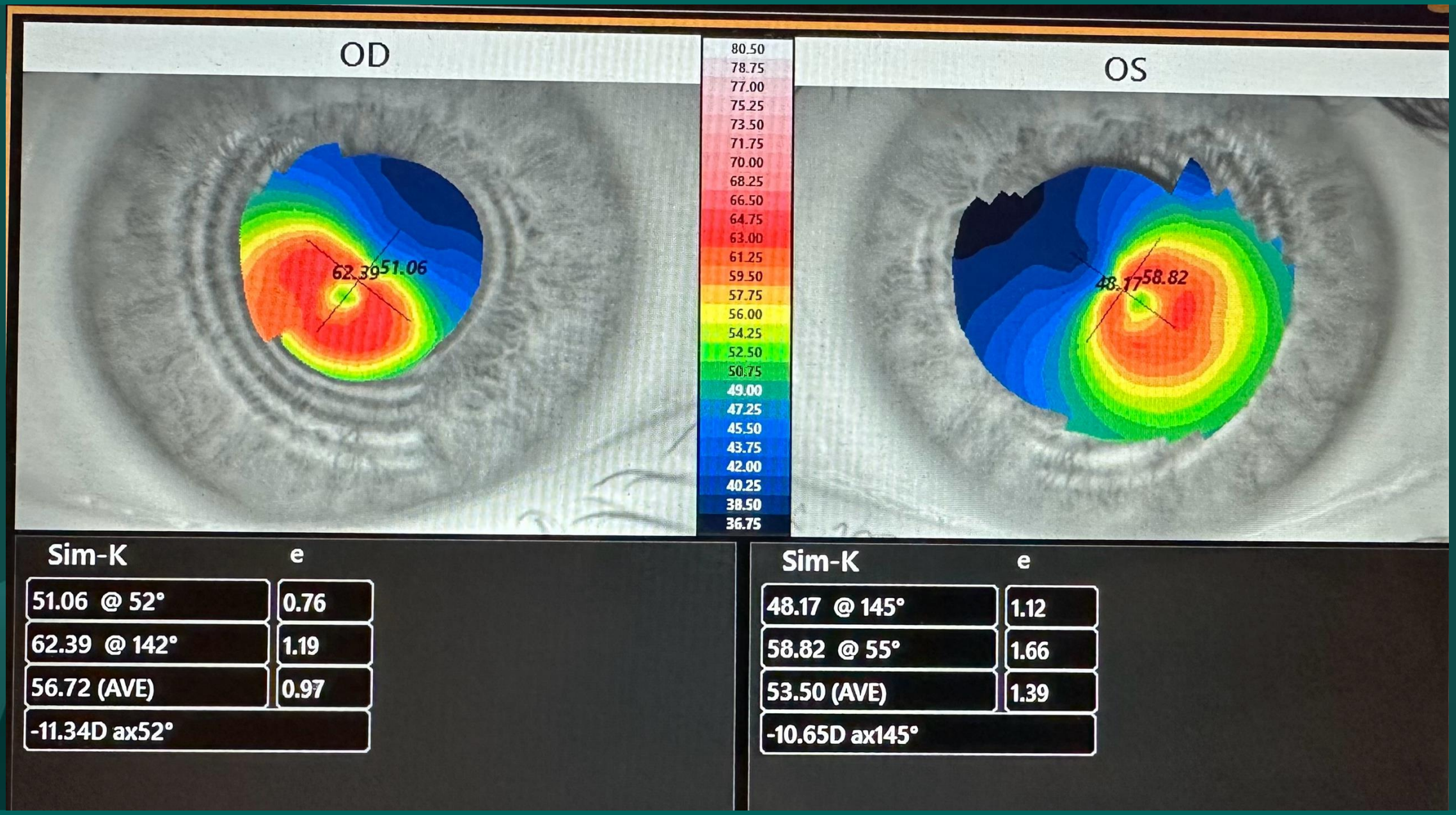
- Still good scleral alignment
- VA cCL
  - OD 20/20
  - OS 20/20
- Minimal to no central clearance
- Ordered new lenses with increased sagittal height and adjusted power

Case 1
1 year later
Plan

- Even with changes in fit, VA 20/15- OD and OS, but he still reports ghosting
- Refer to corneal specialist for cross-linking consultation

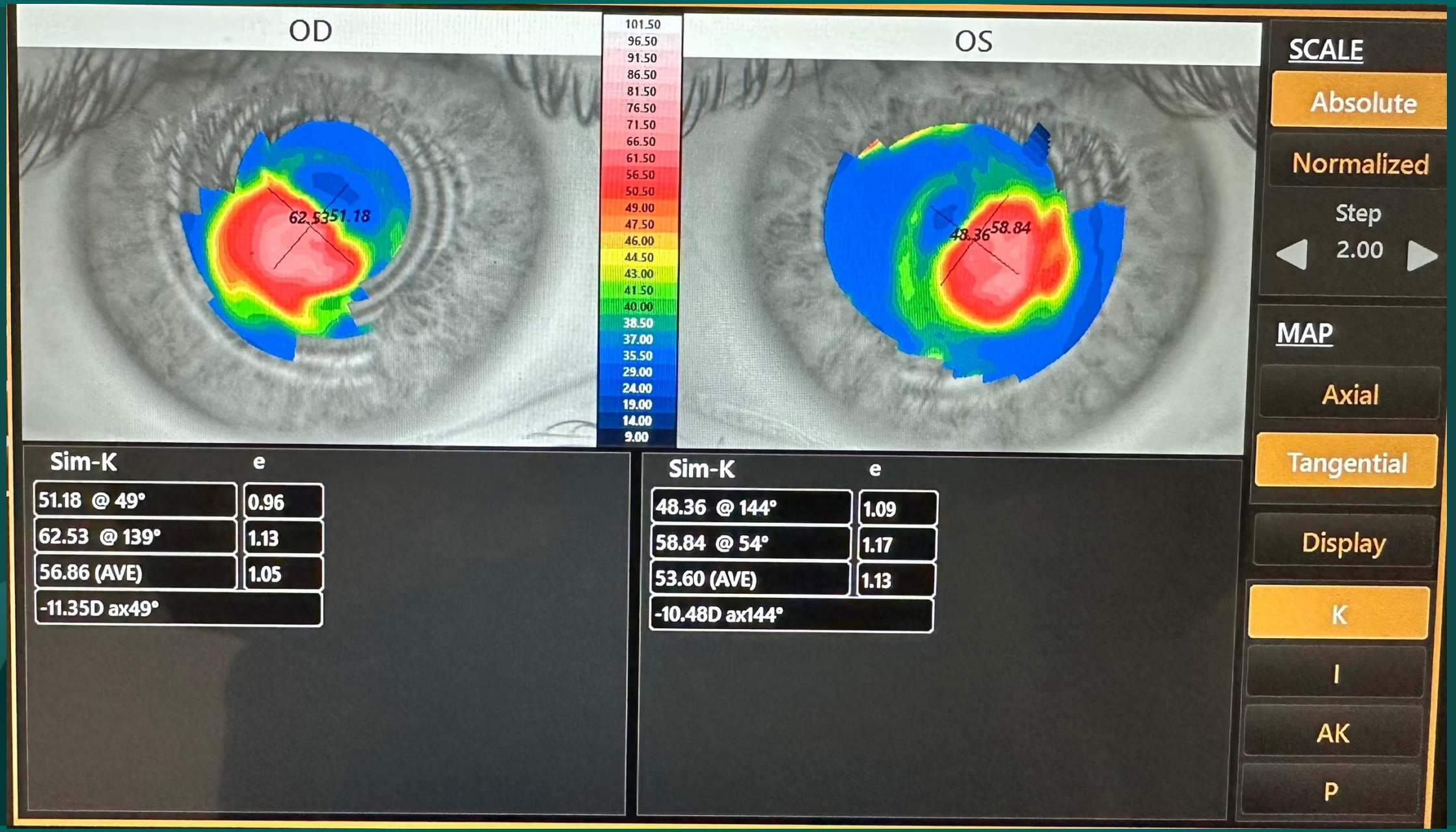
Case 1
4 months later

- The patient's ghosting is getting worse
- VA cCL
  - OD 20/20+
  - OS 20/15-
- Report from corneal specialist
  - "Patient is not progressing fast enough to warrant CXL. Continue to monitor."
- Nothing wrong with the CL fit or the CLs.
- Referred back to corneal specialist to reconsider CXL procedure.


OD
62.39
51.06
80.50
78.75
77.00
75.25
73.50
71.75
70.00
68.25
66.50
64.75
63.00
61.25
59.50
57.75
56.00
54.25
52.50
50.75
49.00
47.25
45.50
43.75
42.00
40.25
38.50
36.75
OS
48.17
58.82
Sim-K
e
51.06 @ 52°
0.76
62.39 @ 142°
1.19
56.72 (AVE)
0.97
-11.34D ax52°
Sim-K
e
48.17 @ 145°
1.12
58.82 @ 55°
1.66
53.50 (AVE)
1.39
-10.65D ax145°

Case 1
Two years later

- He showed 4+ diopters of corneal steepening OD over that time.
- The patient began to grow frustrated with the corneal specialist.
- The ghosting in his right eye was getting worse and worse.
- Finally, the specialist relented and performed epi-off CXL OD.


OD
OS
101.50
96.50
91.50
86.50
81.50
76.50
71.50
66.50
61.50
56.50
50.50
49.00
47.50
46.00
44.50
43.00
41.50
40.00
38.50
37.00
35.50
29.00
24.00
19.00
14.00
9.00
62.53
51.18
48.36
58.84
SCALE
Absolute
Normalized
Step
2.00
MAP
Axial
Tangential
Display
K
I
AK
P
Sim-K
e
51.18 @ 49°
0.96
62.53 @ 139°
1.13
56.86 (AVE)
1.05
-11.35D ax49°
Sim-K
e
48.36 @ 144°
1.09
58.84 @ 54°
1.17
53.60 (AVE)
1.13
-10.48D ax144°

Case 1 Finally

- Three months after CXL, I made a power adjustment to his right lens, and he was back to 20/15 without ghosting.
- He's going to see how it goes over the next year and pursue the left eye at the end of this year.

Corneal Collagen Cross-Linking (CXL)

- FDA approved in April 2016.
- The cornea is bathed in riboflavin (vitamin B_2)
- UV-A radiation is applied for 30 minutes to create oxidative stress
- This causes cross-linking between the collagen and proteoglycans.
- It increases the corneal stiffness 3x and reduces elasticity.

Corneal Collagen Cross-Linking (CXL)

- Cross-linking of collagen side chains and proteoglycan core proteins:
  - Enlarges collagen fibril diameter
  - Reduces interfibrillar spacing
  - Increases stromal stiffness
  - Strengthens cornea
- Increases resistance to enzymatic digestion through:
  - Structural changes making enzyme access harder
  - Increased collagen compaction in anterior stroma

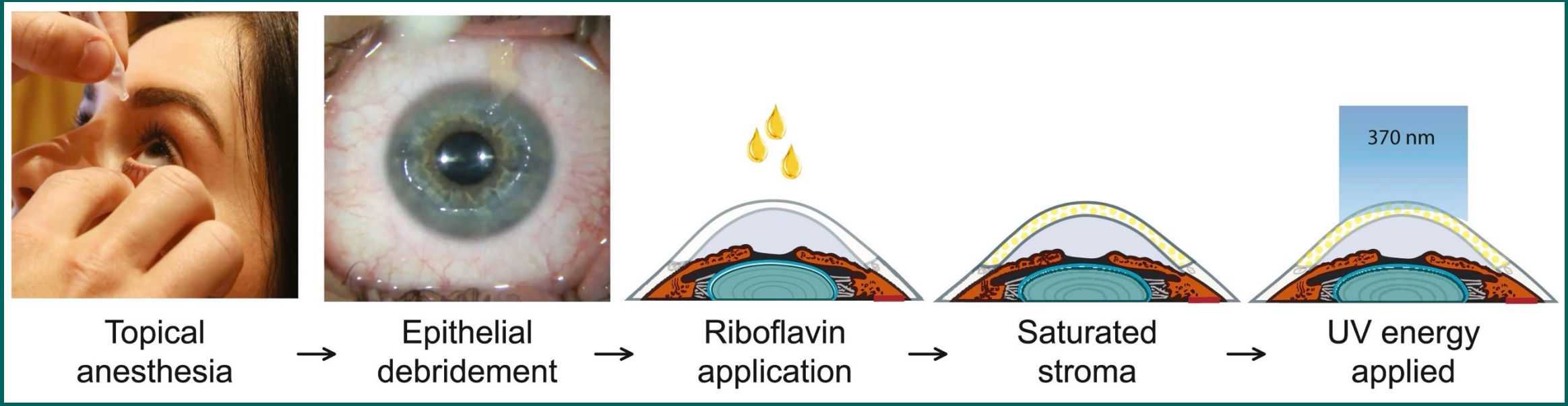
CXL history

- Developed by Theo Seiler, Sr. and Eberhard Spoerl in the 1990s
- Keratoconus corneas are 60-70% weaker than standard corneas because of significantly less cross-linked stromal tissue
- Corneas stiffen with age and in diabetic patients with poor glucose control
- Glycation end-products lead to sugar cross-links
- The idea to use UV light when Seiler went to the dentist – they used UV light to solidify resins used in dental fillings

CXL development

- Riboflavin was chosen because it absorbs a wide range of the light spectrum with peaks at 300 nm and 370 nm.
- 300 nm UV would potentially harm cellular DNA and cause retinal damage
- It was decided 370 nm was a safe compromise

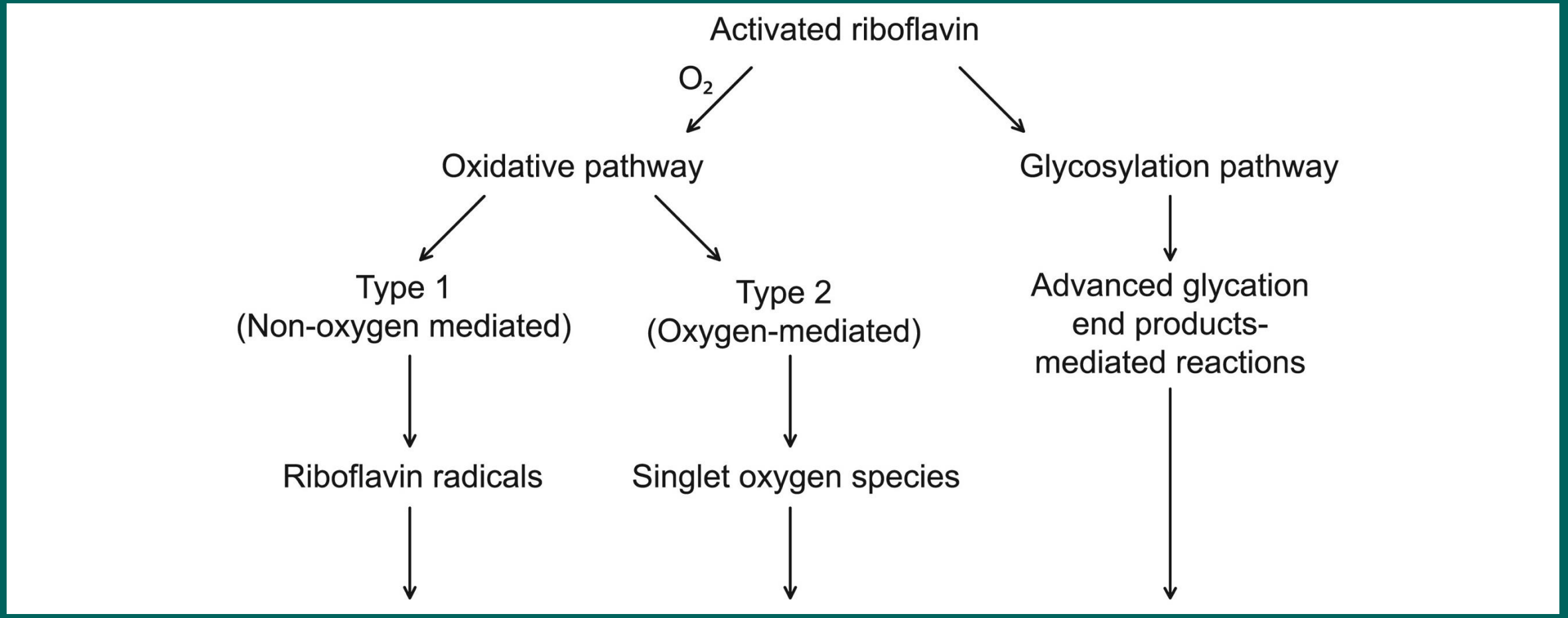
CXL detailed mechanism



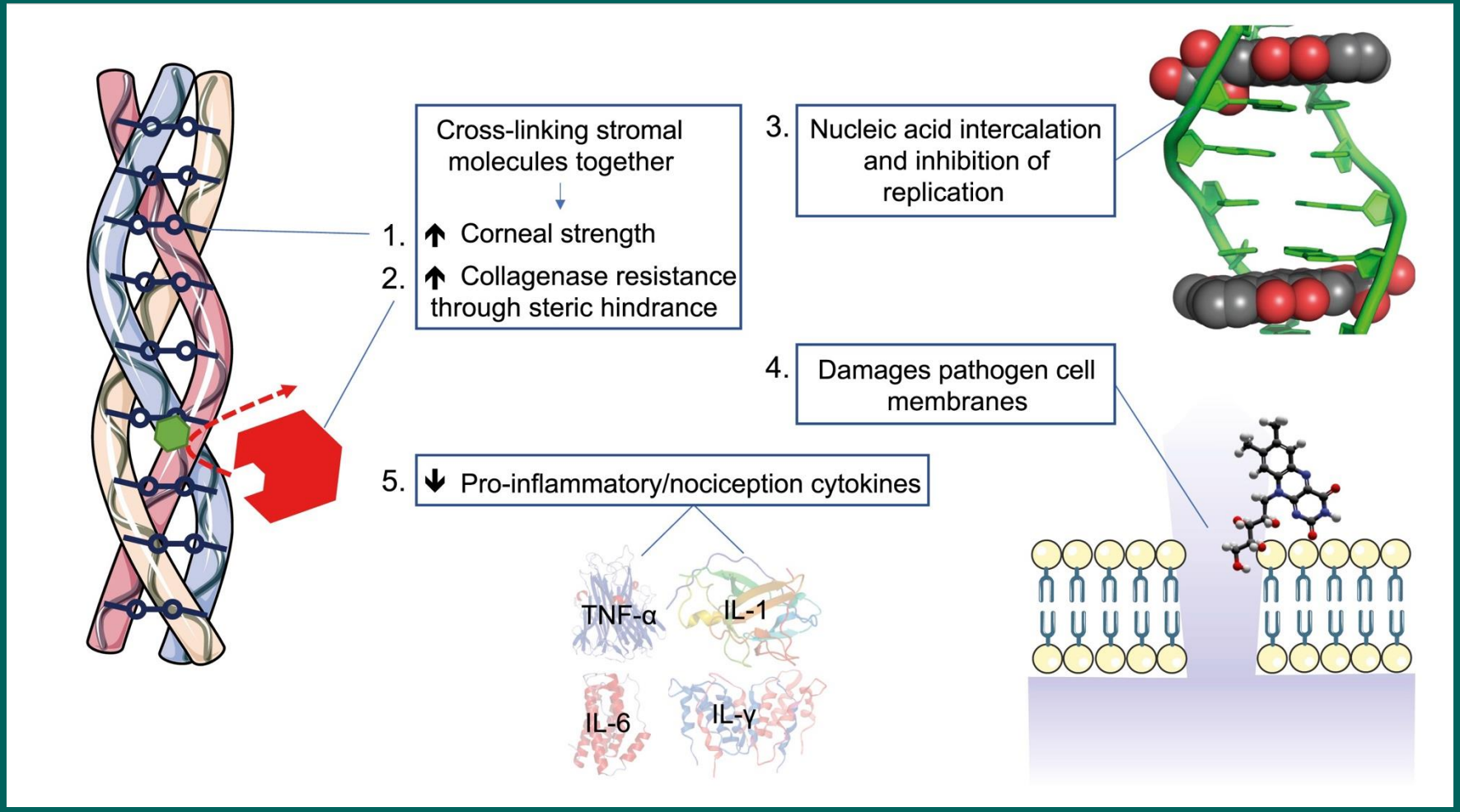
CXL
Dresden Protocol

- Epi-off
- Riboflavin saturation of stroma 30 minutes
- UV-A radiation for an additional 30 minutes
- Required minimum corneal thickness of 400 microns to protect endothelium
- Difficult for riboflavin to pass through the epithelium

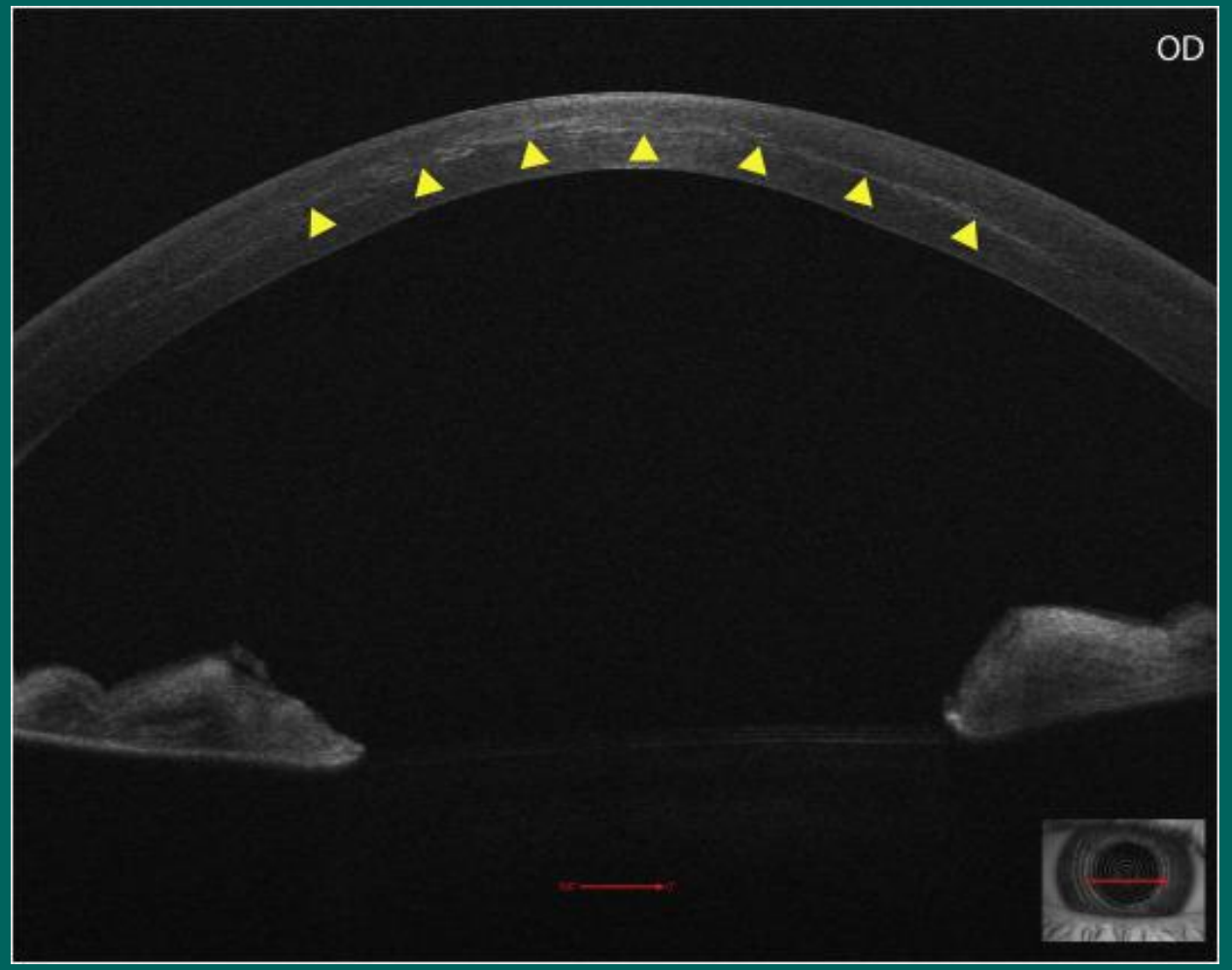
CXL detailed mechanism



CXL detailed mechanism



Demarcation line



CXL
Dresden Protocol

- Dresden protocol limits may be too conservative as higher UV fluences can be safely delivered
- Important to develop optimized epi-off protocol balancing:
  - UV intensity
  - Irradiation time
  - Total fluence
  - Oxygen supply
- Goal is to accelerate procedure while maintaining biomechanical results

CXL
Epi-on vs Epi-off

- Epi-off CXL provides most effective cross-linking results by:
  - Allowing riboflavin to penetrate stroma
  - Avoiding 20% UV absorption from epithelial layer
- Can be used for:
  - Corneal flattening (1–2 D typical effect)
  - Directing higher fluences (up to 10J/cm^2) to steepest regions

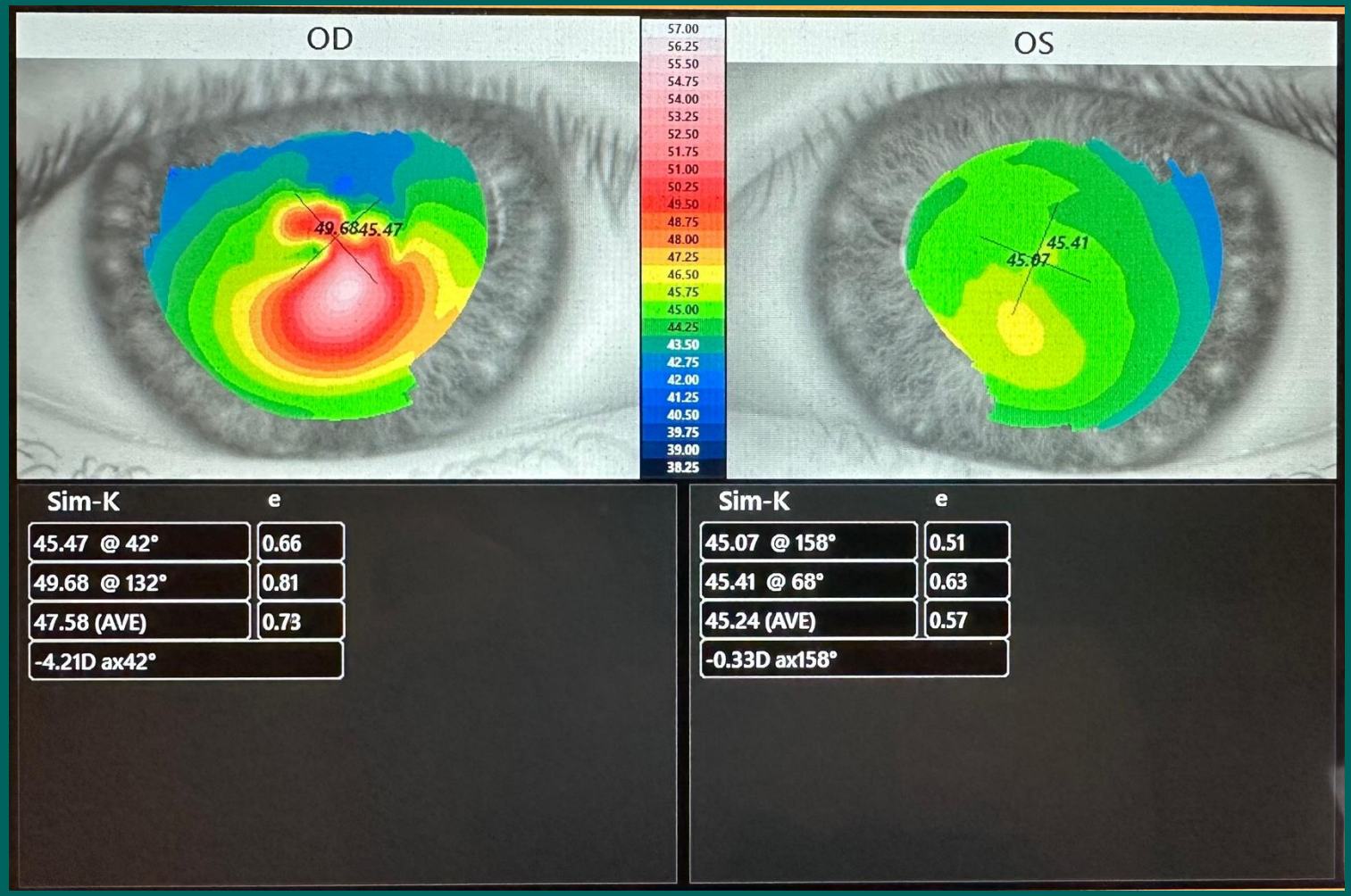
CXL
Epi-on vs Epi-off

- Epi-on protocols
  - Show promising results with oxygen supplementation
  - Lead to less pain and faster healing
  - Quicker recovery of visual acuity

Keratoconus in young people

- More prevalent and aggressive in pediatric and young adult population
- Rates and severity decrease in adulthood
- Natural progression rate is between 77–88% within one year
- Children may not report symptoms until disease is advanced
- 27.8% of children are already at advanced stage at first diagnosis
- Often report rapid decline in visual acuity

12 y/o first eye exam



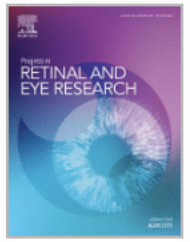
Keratoconus in young people

- Early detection and intervention with CXL is crucial
- Some surgeons advocate immediate CXL upon detection rather than waiting for progression
- Frequent follow-ups recommended every 1–3 months
- From the "Siena CXL Pediatrics" study (ages 10–18):
  - Showed significant and rapid functional improvement after CXL
  - No severe adverse effects recorded
  - CXL effectively slowed keratoconus progression in 80% of patients for up to three years
  - However, 4.6% exhibited deterioration during follow-up due to aggressive nature of keratoconus in this demographic

Great review paper

Progress in Retinal and Eye Research

Volume 104, January 2025, 101322



Corneal cross-linking

Farhad Hafezi [a b c d e f], Sabine Kling [g], Nikki L. Hafezi [a b f h], M. Enes Aydemir [a b], Nan-Ji Lu [a b h i], Mark Hillen [a], Boris Knyazer [j], Shady Awwad [k], Cosimo Mazzotta [l], Léonard Kollros [a m], Emilio A. Torres-Netto [a b c]

Case 2
Visit 1
Comprehensive Exam

- 68 y/o white female presented with a complaint of blurred vision in both eyes that started 4-6 weeks prior
- History of LASIK OS 1.5 years prior for distance correction. No treatment OD for monovision effect
- History of RGP wear but has not worn for 8 years since going through chemotherapy for breast cancer. She has had dry eye since then.

Case 2 Visit 1 History

- Current systemic medication: Arimidex
- Current ocular medication: no prescribed eye drops, only uses artificial tears
- Her dry eye has gotten worse as her vision has gotten blurrier recently. She wakes up in the morning with significant dried mucous on her lids. She also has been getting white dry mucous throughout the day.

Case 2
Visit 1
Entrance Testing
Refraction

- VA sc
  - OD 20/80
  - OS 20/70
  - OU 20/60
- Pupils ERRL D&C –APD
- EOMs SAFE
- Refraction
  - OD -1.50 -0.50 x 036 20/25
  - OS +1.00 -0.75 x 054 20/60

Case 2
Visit 1
Slit lamp

- L/L OU: 2+ lid margin hyperemia, MG drop out with thick secretions
- Conj OU: 1+ diffuse injection
- Cornea
  - OD: clear
  - OS: 3+ central SPK; superior hinge LASIK scar
- A/C OU: D&Q
- Lens OU: 1+ NSC
- Fundus exam unremarkable OU

Case 2
Visit 1
Slit lamp

- L/L OU: 2+ lid margin hyperemia, MG drop out with thick secretions
- Conj OU: 1+ diffuse injection
- Cornea
  - OD: clear
  - OS: 3+ central SPK; superior hinge LASIK scar
- A/C OU: D&Q
- Lens OU: 1+ NSC
- Fundus exam unremarkable OU

Case 2
Visit 1
Assessment/Plan

- Meibomian gland dysfunction OU
  - Discussed referral for Lipflow treatment
- Dry Eye Syndrome OU
  - Started on PFATs 4-5x/day
- Punctate Keratits OS
  - Rx prednisolone acetate QID OS and f/u in 1 week
- Age-related nuclear cataract OU
  - Monitor

Case 2
Visit 2
History/Entrance Testing

- She has been using the drops as instructed.
- They burn when she puts them in OS.
- She is still getting white mucous OS intermittently throughout the day
- Vision is still blurry, but it feels like it is improving
- VA sc:
  - OD 20/70 PH 20/25
  - OS 20/50 PH 20/25

Case 2
Visit 2
Anterior Segment Update

- Conj OU: tr diffuse injection
- Cornea
  - OD: 1+ central SPK
  - OS: 2+ central SPK

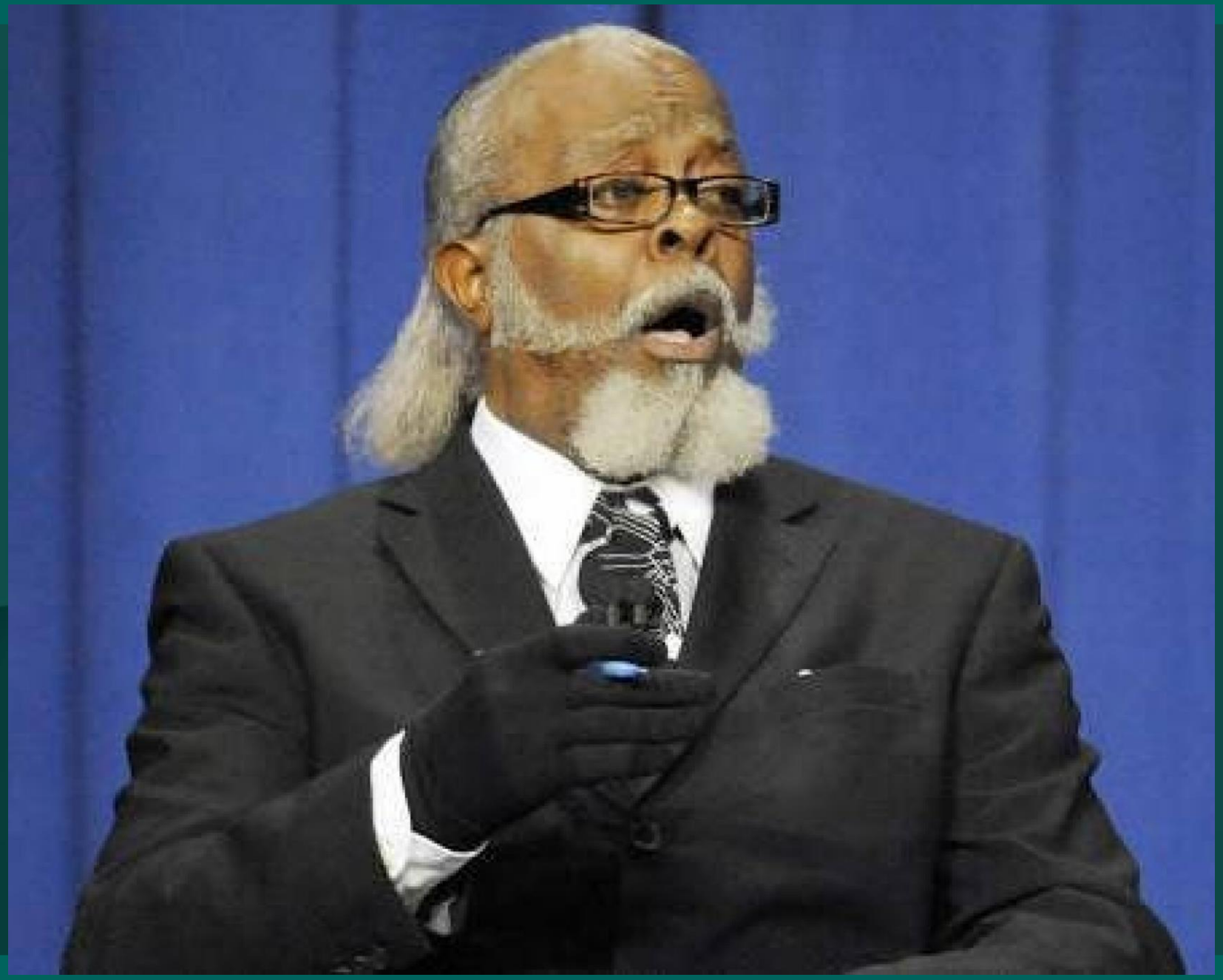
Case 2
Visit 2
Assessment/Plan

- Punctate keratitis OS>OD – improving OS w/ dry eye syndrome OU
  - Reduce pred acetate to BID OS x 1 week
  - PFATs TID OU and Systane Night Gel QHS OU
  - Discussed starting Restasis and Lipiflow referral
  - Monitor in 3-4 weeks

Case 2 Visit 3 Overall summary

- Continues to use PFATs and nighttime gel as instructed
- Vision improving though has good days and bad days
- VA sc:
  - OD 20/100 PH 20/25
  - OS 20/30
- Cornea:
  - OD tr central SPK
  - OS persistent 2+ central SPK
- TBUT 2-3 sec OU
- D/C nighttime gel, begin Restasis BID OU, continue with PFATs 2-3x/day OU
- Refer for Lipiflow


Three
Months
Later...



Case 2 Visit 4 History

- She went for Lipiflow consultation but did not pursue as it was cost prohibitive for her
  - Was started on hot compress mask QHS w/ lid scrubs
- She did not start the Restasis because even with her insurance, the cost was too high.
- She was taking the PFATs 4-5x/day
- She feels like vision is stable since her last visit, but it fluctuates throughout the day
- VA sc
  - OD 20/150
  - OS 20/80

Case 2
Visit 4
Cornea/Plan

- OD 2+ scattered SPK – mostly inferior
- OS 4+ diffuse SPK covering the entire central 10 mm
- Rx loteprednol 0.5% QID x 2 weeks

Case 2
Visit 5

- Taking drops as directed and feels better
- VA sc
  - OD 20/80
  - OS 20/40
- SLE cornea
  - OD 1+ inf SPK
  - OS 2+ diffuse SPK
- Plan
  - Patient was just about to go on a trip
  - Reduce loteprednol to BID with PFATs prn throughout the day
  - Follow up in 2 weeks when she returns from her trip

Case 2
Visit 6

- She feels fine, but vision is still blurry. Mildly better than before her trip.
- VA sc
  - OD 20/80
  - OS 20/30
- SLE cornea
  - OD 1+ inf SPK
  - OS 2+ diff SPK

Case 2
Visit 6

- Inserted 9 mm freeze-dried amniotic membrane OS under BCL
- d/c loteprednol
- Use PFATs qid OU
- RTC 6 days for BCL removal

Case 2
Visit 7
BCL removal

- Removed BCL without complication
- OS cornea
  - 1+ diffuse epithelial edema
- Instructed to use loteprednol bid x 1 week OS then d/c
- PFATs qid
- Monitor 3 months

Case 2
Visit 8
3 months later

- Her eyes feel fine. Vision is getting a little worse.
- Using PFATs 6-8 times per day OU
- Medical history stable
- VA sc
  - OD 20/80
  - OS 20/50
- SLE cornea OS
  - 2+ diffuse central SPK

Case 2
Visit 8 treatment

- Rx Oxervate (Dompe) 6 times/day for 8 weeks

Case 2
Visit 9
2 weeks s/p starting Oxervate

- She has been taking drops as directed
- She noted significant redness OS for the first 6-7 days which has been improving.
- She has had burning which didn't start until after 10 days of treatment. Not unbearable, but enough to use cold compresses.

Case 2
Visit 9
2 weeks s/p starting Oxervate

- VA sc
  - OD 20/80
  - OS 20/40
- SLE OS
  - Conj: 1+ diff injection
  - Cornea: 2+ confluent SPK
- Continue Oxervate and ATs
- Recommend 1000 mg acetaminophen q6h prn for pain
- Monitor every 2 weeks while on therapy

Case 2 Progress summary and results

- After therapy was complete, the patient reports good comfort and vision.
- VA sc
  - OD 20/80
  - OS 20/25
- SLE cornea
  - OD tr inf SPK
  - OS clear
- Instructed to take PFATs 2-4x/day OU
- Pt moved to NY to be closer to family

Neurotrophic keratitis (NK)

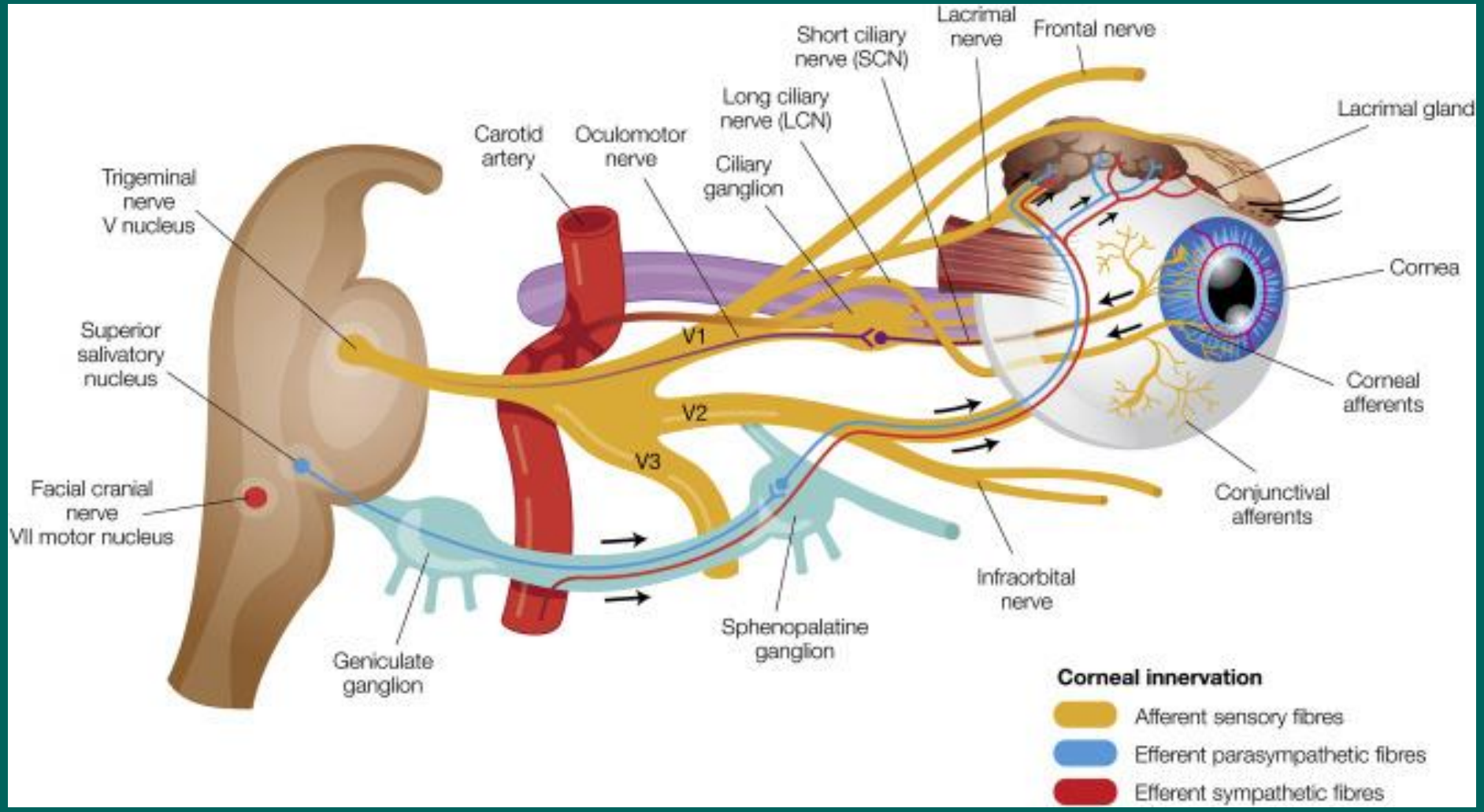
"Neurotrophic keratopathy (NK) is a degenerative disease of the corneal epithelium resulting from impaired corneal innervation. A reduction in corneal sensitivity or complete corneal anaesthesia is the hallmark of this disease and is responsible for producing epithelial keratopathy, ulceration and perforation"

-- American Academy of Ophthalmology (2008)

NK history

- Was first described by Magendie in 1824
- Neurotrophic ulcers in the skin were identified by Dubler in 1884
- Corneal changes were found after trigeminal nerve damage
- Thought to alter cell metabolism which leads to cell death and a trophic ulcer

Anatomy


Short ciliary nerve (SCN)
Lacrimal nerve
Frontal nerve
Long ciliary nerve (LCN)
Lacrimal gland
Carotid artery
Oculomotor nerve
Ciliary ganglion
Trigeminal nerve V nucleus
Cornea
Superior salivatory nucleus
V1
V2
V3
Corneal afferents
Facial cranial nerve VII motor nucleus
Conjunctival afferents
Infraorbital nerve
Sphenopalatine ganglion
Geniculate ganglion
Corneal innervation
Afferent sensory fibres
Efferent parasympathetic fibres
Efferent sympathetic fibres

Corneal nerve physiology

- Polymodal nociceptor neurons
  - Mechanical (intense pressure, stretching)
  - Thermal (extreme heat or cold)
  - Chemical (inflammatory mediators, acids, irritants)
- Stimulation of these receptors lead to
  - Sensitization causing pain
  - Reflex tearing

Corneal nerve physiology

- 20-30% of axons respond to pain
- 10-15% respond to temperature
- Corneal nerves work in concert with the immune system to maintain a healthy corneal surface

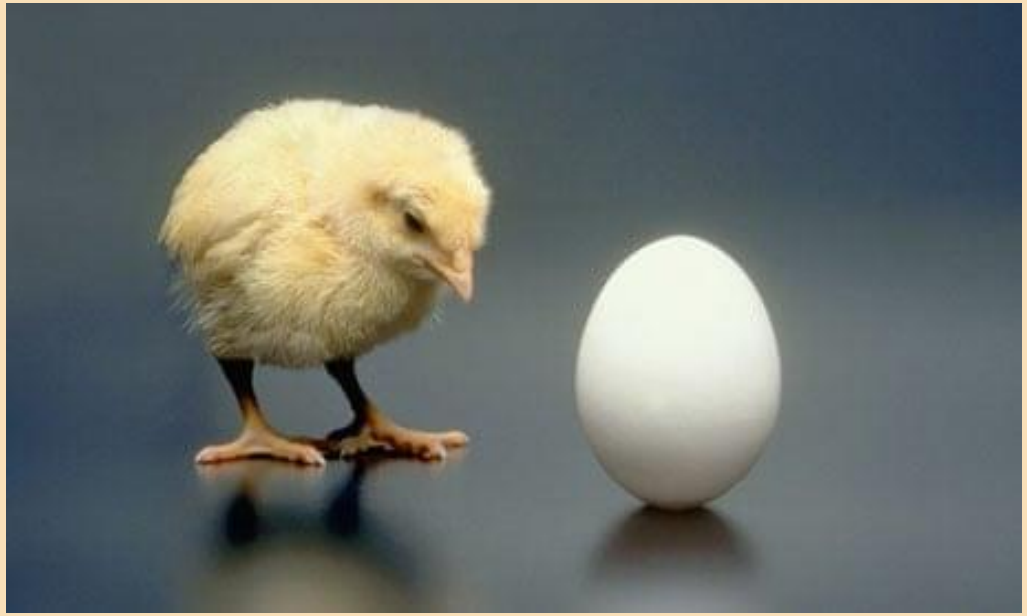
NK prevalence

- Based on its original definition it is classified as a rare/orphan disease
  - Affecting less than 5 in 10,000 people
- Most likely this is a low estimate
- However, there is no consensus
- NK develops
  - 6% of herpes simplex keratitis
  - 13% of herpes zoster keratitis
  - 3% post-surgical trigeminal nerve damage

Causes of NK

- Ocular
  - Herpes infection
  - Chemical burn
  - Chronic surface inflammation
  - Laser refractive surgery
- CNS
  - Tumor
  - Degenerative CNS disorders
  - Trigeminal nerve injury
- Systemic disease
  - Vitamin A deficiency
  - Diabetes
  - MS
  - Leprosy
- Genetic disorders
  - Riley-Day syndrome
  - Goldenhar-Gorlin syndrome
  - Mobius syndrome

NK and dry eye



NK has a dry eye component, and chronic dry eye can lead to NK. LASIK leads to neuropathic dry eye in 2-5% of Caucasian patients.

NK pathogenesis

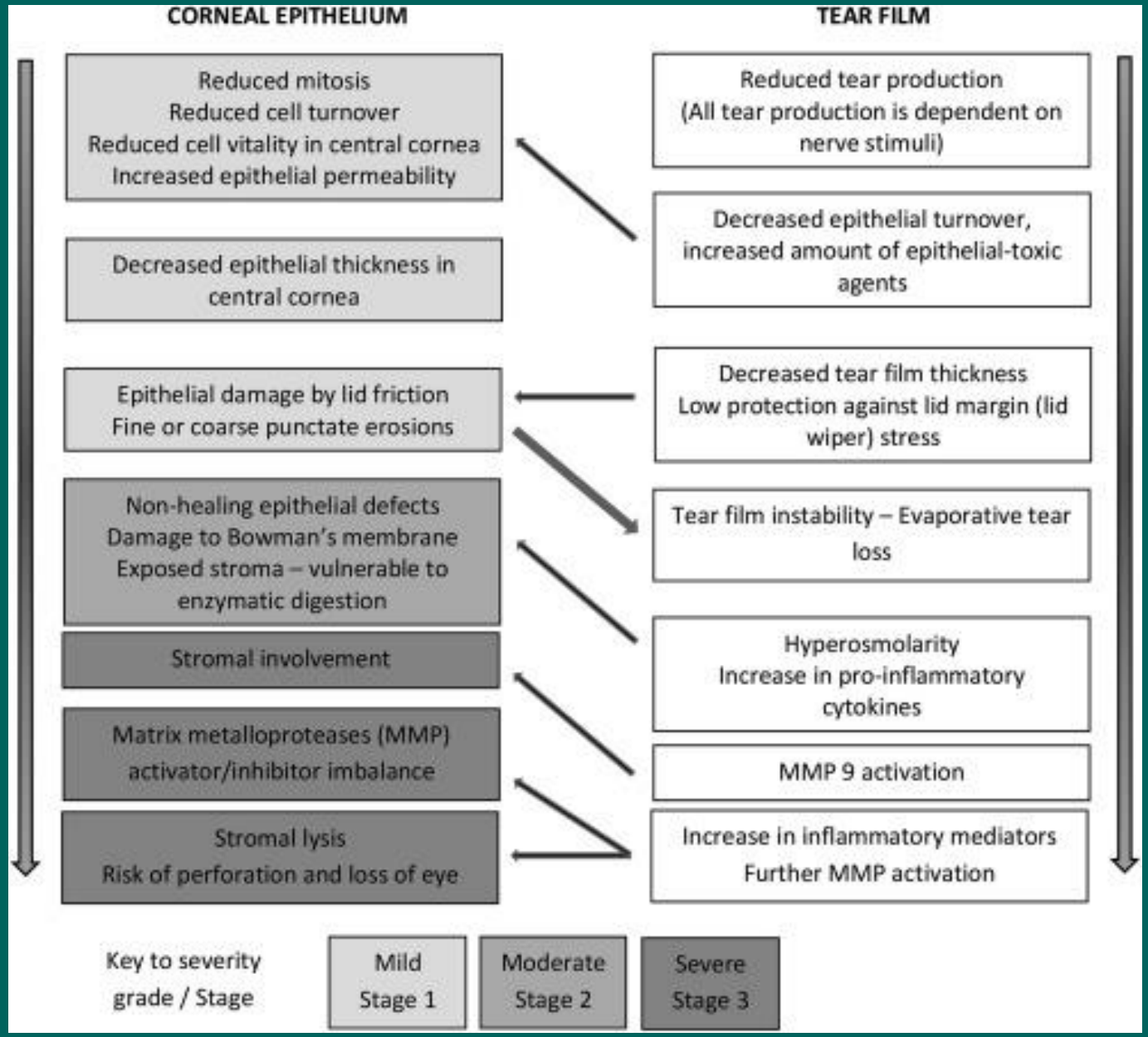
- Combination of factors
  - Decreased lacrimation because of reduced nerve stimulus
  - Impaired blink reflex due to lack of corneal sensitivity
  - Abnormal cell metabolism secondary to loss of trophic influences

NK pathogenesis

- Rapid TBUT causes a drop in corneal temperature
  - Chronic drops in corneal temperature can lead to desensitization
- Lack of tear production reduces neurogenic growth factor (NGF)
  - Leads to reduced mitosis of corneal epithelial cells
  - Reduced migration of cells in the corneal affecting the central cornea the most
  - Reduced ability to hold the tears on the ocular surface
  - Reduced clearance of pro-inflammatory cytokines

NK pathogenesis vicious cycle

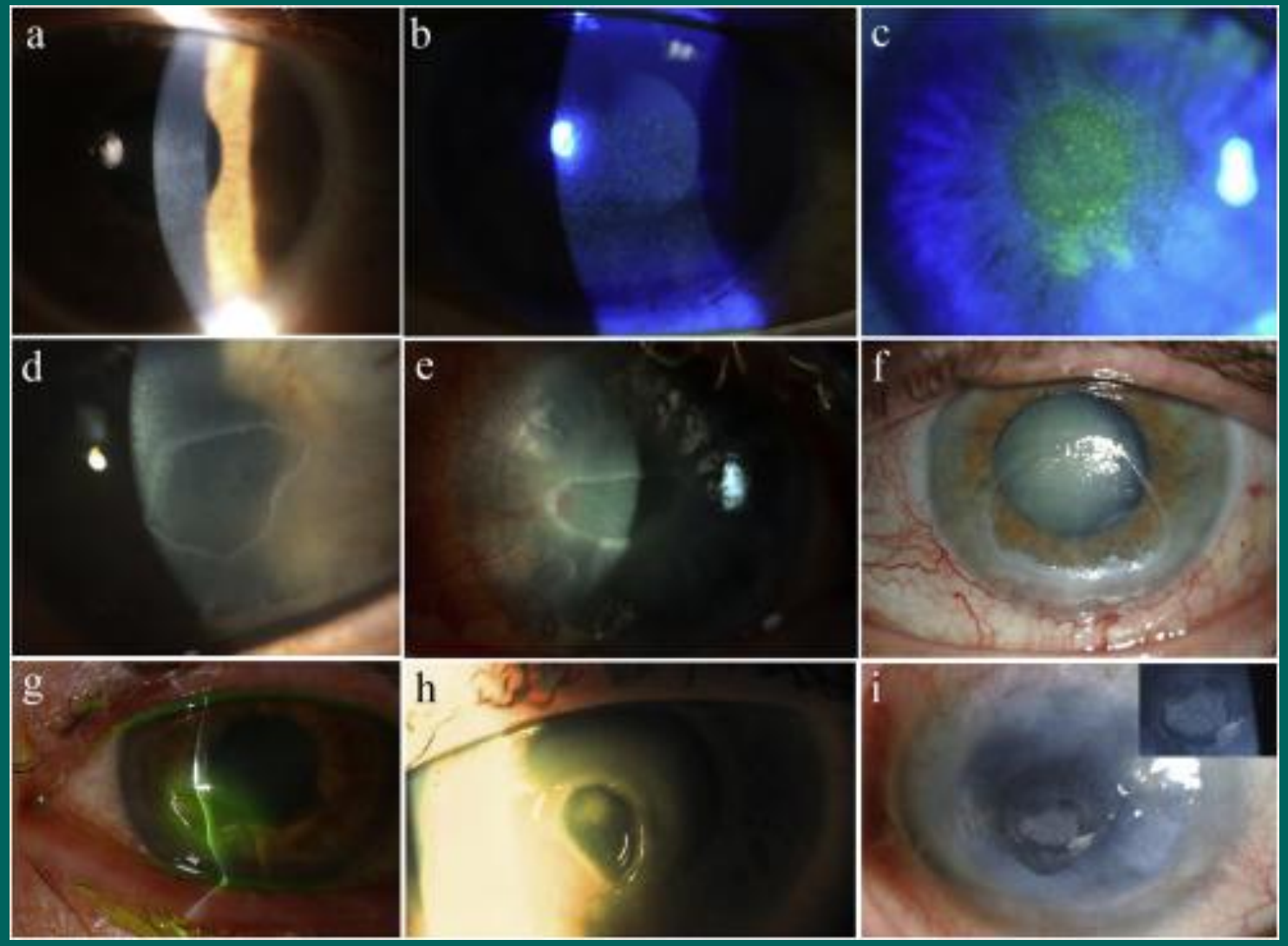
- Epithelial cell damage makes nerves more susceptible to damage
- More tear evaporation
- More nerve stimulation
- Neurogenic inflammation
- More epithelial damage
- Loss of nerve sensitivity leads to less tear production
- Hyperosmotic environment inducing cell death and more inflammation
- Increased matrix metalloproteinases (MMP)


CORNEAL EPITHELIUM
TEAR FILM
Reduced mitosis
Reduced cell turnover
Reduced cell vitality in central cornea
Increased epithelial permeability
Reduced tear production
(All tear production is dependent on nerve stimuli)
Decreased epithelial turnover, increased amount of epithelial-toxic agents
Decreased epithelial thickness in central cornea
Epithelial damage by lid friction
Fine or coarse punctate erosions
Decreased tear film thickness
Low protection against lid margin (lid wiper) stress
Non-healing epithelial defects
Damage to Bowman's membrane
Exposed stroma – vulnerable to enzymatic digestion
Tear film instability – Evaporative tear loss
Stromal involvement
Hyperosmolarity
Increase in pro-inflammatory cytokines
Matrix metalloproteases (MMP) activator/inhibitor imbalance
MMP 9 activation
Stromal lysis
Risk of perforation and loss of eye
Increase in inflammatory mediators
Further MMP activation
Key to severity grade / Stage
Mild
Stage 1
Moderate
Stage 2
Severe
Stage 3

BAK and NK

- Cytotoxic properties
  - Can induce pro-inflammatory and pro-apoptotic events
- Has been shown to be neurotoxic
- May negatively affect corneal wound healing
- Should be considered in cases of chronic poor wound healing in treated patients

Diagnosing NK



Standard classification of NK

- The Mackie System
  - Stage 1 – mild; limited to the superficial corneal epithelium; decreased TBUT; maybe inferior corneal vascularization
  - Stage 2 – moderate; deeper persistent epithelial defect with smooth, rolled edges
  - Stage 3 – severe; corneal ulcer with stromal melt

Updated classification of NK

- Neurotrophic Keratopathy Study Group
  - Stage 1 is reduced corneal sensitivity without significant corneal signs.
  - Stage 2 has superficial epithelial keratitis but there is no stromal involvement.
  - Stage 3 is when stage 2 is recurrent.
  - Stage 4 is when there are epithelial defects associated with stomal involvement.
  - Stage 5 is when a corneal ulcer is present.
  - Stage 6 occurs when the corneal ulcer progresses to perforation.

Treatment of NK Mild

- PFATs
- Punctal occlusion
- Treat lid issues (MGD, etc)
- Topical steroids
- Restasis/Xiidra/Cequa

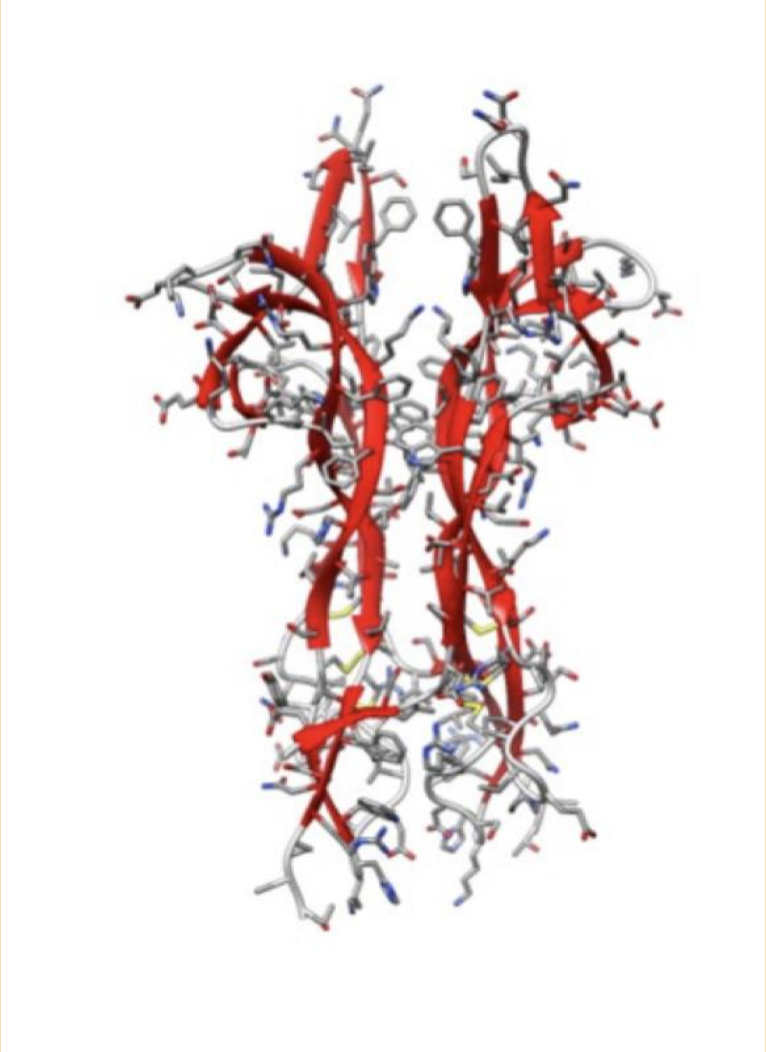
Treatment of NK Moderate

- Everything in mild plus
- PF topical antibiotics
- Oral doxycycline to fight corneal melt
- Serum eye drops/PRP
- Bandage CL or scleral CL fitting
- Tarsorrhaphy
- Amniotic membrane
- Cengenermin/Oxervate

Treatment of NK Severe

- Everything in mild and moderate plus
- Cengenermin/Oxervate
- Amniotic membrane graft
- Cyanoacrylate with BCL

Treatment of NK Cenegermin-bkbj (Oxervate)



- Oxervate is a novel recombinant human growth factor which is identical to real NGF protein

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