

Pharmaceutical Treatment of Anterior Segment Inflammatory Conditions

Mile Brujic, OD, FAAO

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Unfortunately, the speaker has no financial or proprietary interest in any of the products that are mentioned

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 - **Premier Vision Group**
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Tools to Control Inflammation

Non-Steroidal Anti-inflammatory Drug (NSAID)

- Provides analgesic, antipyretic and anti-inflammatory effects
- Inhibits cyclooxygenase
 - COX-1 and COX-2
 - COX-1 – normal physiological response (stomach)
 - COX-2 – facultatively expressed - inflammation
- COX produces prostaglandins and thromboxanes from arachidonic acid

Tools to Control Pain

Non-Steroidal Anti-inflammatory Drug (NSAID)

- May Slow or delay wound healing
- Epithelial breakdown
- Corneal thinning
- Corneal erosion
- Corneal ulceration
- Corneal perforation

Tools to Control Pain

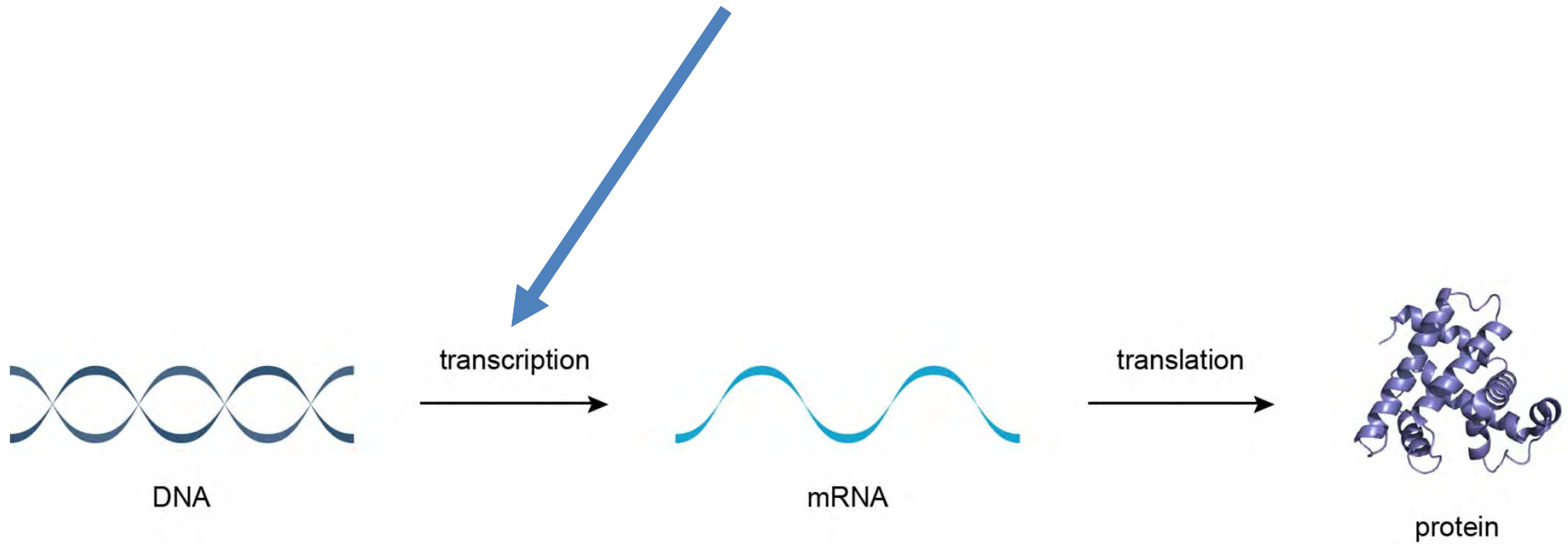
Non-Steroidal Anti-inflammatory Drug (NSAID)

- Bromfenac 0.075% (Bromsite – SunPharma)
- Bromfenac 0.09% (Bromday), 0.07% (Prolensa) – both are qd dosing regimen
- Ketorolac Tromethamine 0.5% (Acular), 0.4% (Acular LS), 0.45% (Acuvail – qd/pf)
- Nepafenac 0.1% (Nevanac tid); 0.3% (Ilevro qd)

Tools to Control Pain

- Steroids
 - Steroid receptors complex influence DNA transcription in the nucleus of the cell
 - Inhibits transcription of COX-2, cytokines, cell adhesion molecules
 - Inhibits edema, fibrin deposition, capillary dilation, and phagocytic migration, and scar formation.


Steroids affect this step



Treatment Options



Fluorometholone modulates gene expression of ocular surface mucins

Jonathan Taniguchi and Ajay Sharma 

Department of Biomedical and Pharmaceutical Sciences, Chapman University School of Pharmacy, Chapman University, Irvine, CA, USA

ABSTRACT.

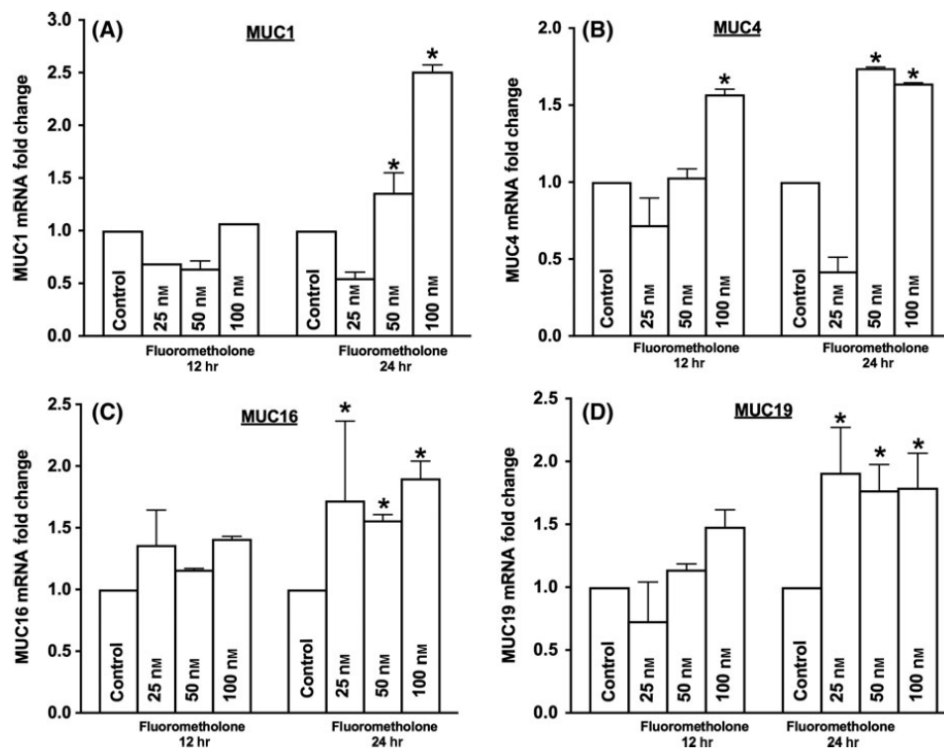
Purpose: Mucins are vital to keep the ocular surface hydrated. Genes encoding for mucins contain a glucocorticoid response element. The purpose of this study was to evaluate the effect of fluorometholone, a glucocorticoid receptor agonist used in the management of dry eye, on the gene expression of conjunctival and corneal epithelial cell mucins.

Methods: Stratified cultures of human conjunctival and corneal epithelial cells were exposed to 25, 50 and 100 nM of fluorometholone alone or in presence of mifepristone, a glucocorticoid receptor antagonist. The mRNA was isolated from the cells and reverse transcribed to cDNA. The cDNA was used for quantification of gene expression of mucin (MUC) 1, 4, 16 and 19 using real-time PCR.

pathogens and keeping the organ surface hydrated. Mucins can be tethered to the cell membrane of epithelial cells or can be secreted. The ocular surface expresses 3 membrane-bound mucins (MUC), MUC1, MUC4, MUC16; one secreted mucin, MUC19; and one gel-forming secreted mucin, MUC5AC (Gipson & Argüeso 2003; Gipson 2004; Ablamowicz & Nichols 2016). The membrane-bound mucins are

Mucin Gene Expression with Fluorometholone

Human Conjunctival and Corneal Epithelial Cells



Real-time PCR quantification of gene expression in human conjunctival epithelial cells treated with fluorometholone (25, 50 and 100 nM) for 12 and 24 hr.

(A) - MUC1

(B) - MUC4

(C) - MUC16

(D) - MUC19

*p < 0.05 compared to control

Taniguchi J., Sharma A.. Fluorometholone modulates gene expression of ocular surface mucins. Acta Ophth 1-7:2019.

Ointments



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- Lee, Los Angeles, CA

Drug Name


fluorometholone

Location

43402

FIND THE LOWEST PRICE

Drug prices are different at every pharmacy.
How GoodRx helps:



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http://www.goodrx.com/fluorometholone/price

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Drug Prices | What is fluorometholone? | Side Effects | Photos

Prices for 1 5ml eye dropper of fluorometholone 0.1% (generic)

Share

Save to My Prescriptions

Location

within 6 miles

fluorometholone (generic)

Form

Eye Dropper

Dosage

5ml of 0.1%

10ml of 0.1%

15ml of 0.1%

Rite-Aid

\$8.02 with coupon

Save 55% vs. cash price

Get Coupon

Walgreens

\$9.72 with coupon

Save 48% vs. cash price

Get Coupon

Kroger Pharmacy

\$11.34 with coupon

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Meijer Pharmacy

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Save 50% vs. cash price

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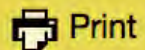
Walmart

\$12.04 with coupon

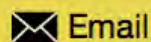
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fluorometholone 5ml

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Topical corticosteroids



Patient Programs

<https://myflarex.com/copay-program/>

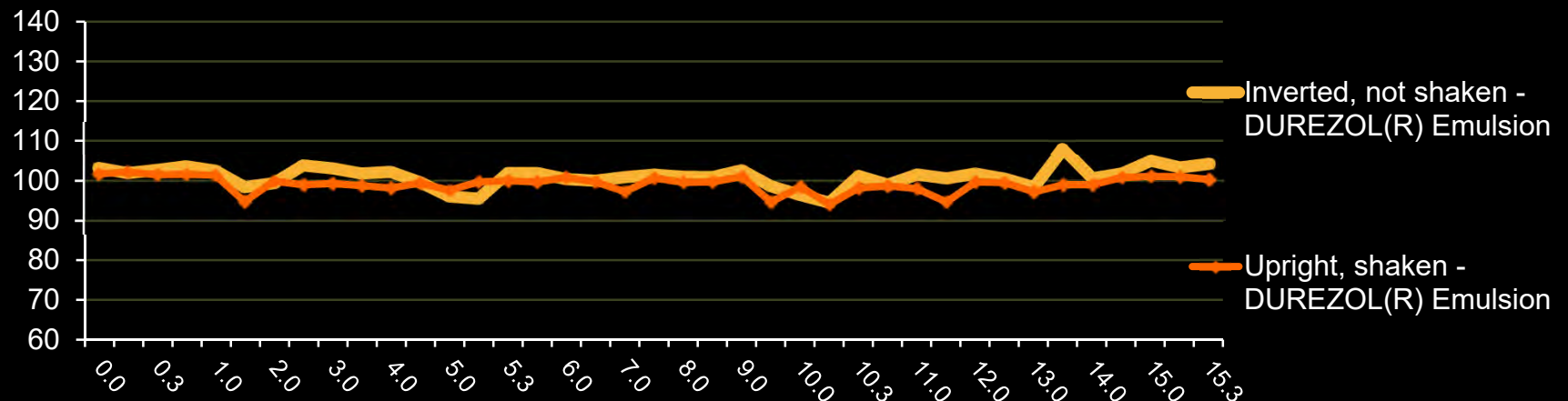
<https://www.lotemaxsm.com/patient/savings>

<https://www.scripthero.com/search/medication/DUREZOL>

<https://inveltys.com/>

Tools to Control Pain

- Steroids
 - Durezol
 - Preserved with sorbic acid
 - Provides drop to drop uniformity



DUREZOL[®] EMULSION:

US Pivotal Phase 3 Studies in endogenous Anterior Uveitis

- Two, phase 3, randomized, double-masked studies of DUREZOL[®] Emulsion compared to Pred Forte* (prednisolone acetate suspension) 1% for the treatment of endogenous anterior uveitis
- Inclusion Criteria
 - Noninfectious anterior uveitis in at least 1 eye
 - Anterior chamber cell grade ≥ 2 (≥ 11 cells) and a flare score ≥ 2 (more than moderate) in same eye
 - ≥ 2 years old on day of consent

*Trademark is the property of its owner

1. Foster CS, Davanzo R, Flynn TE, McLeod K, Vogel R, Crockett RS. DUREZOL[®] (Difluprednate Ophthalmic Emulsion 0.05%) Compared with PRED FORTE[®] 1% Ophthalmic Suspension in the Treatment of Endogenous Anterior Uveitis. *J Ocul Pharmacol Ther.* 2010 Oct;26(5):475-83.
2. Data on file, Alcon Laboratories, Inc.

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Novartis |
DUR13153SK
|Nov 2013|19

Study Design^{1,2}

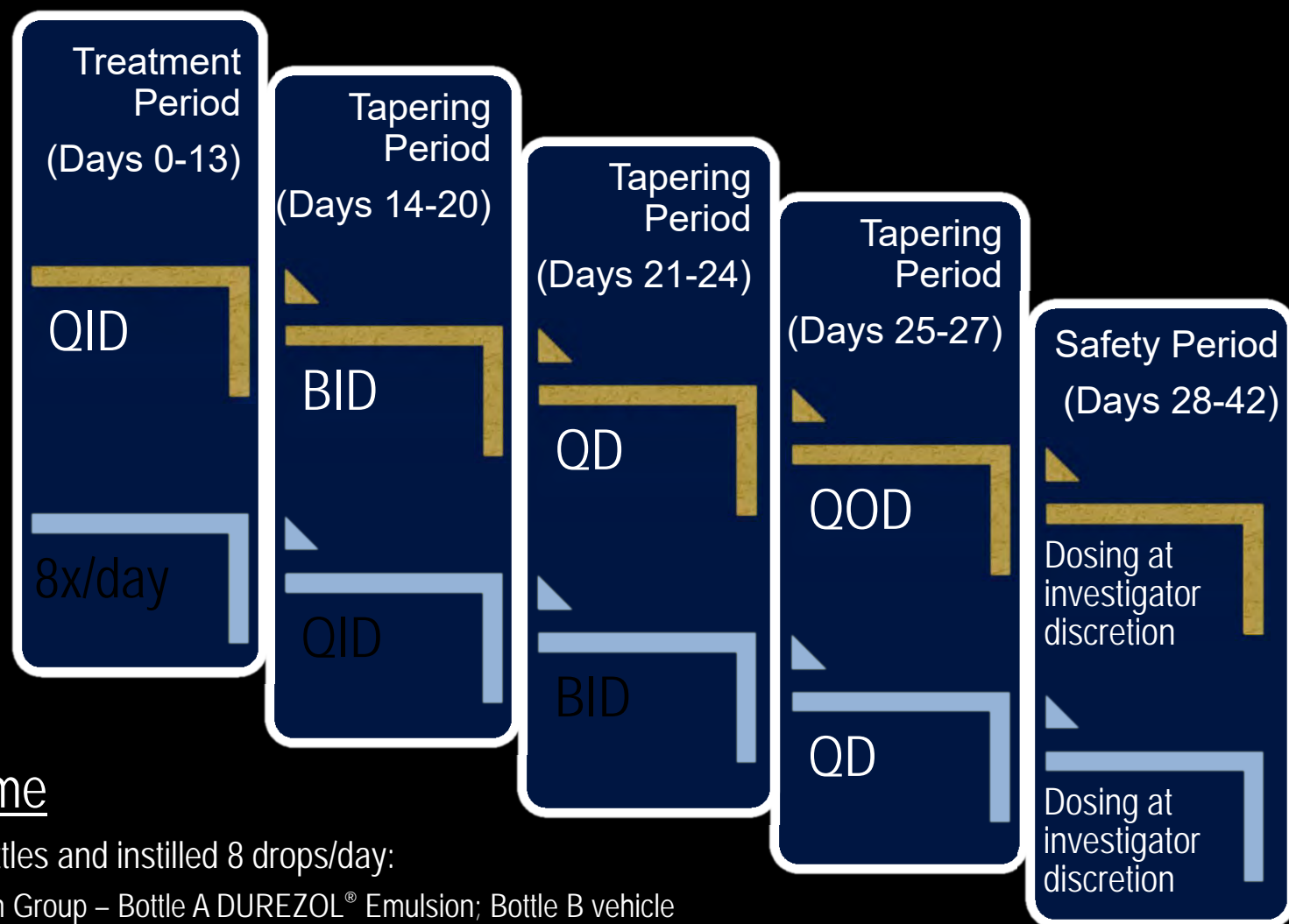
**DUREZOL®
Emulsion**

**Pred Forte*
Suspension**

Masking Scheme

All patients given 2 bottles and instilled 8 drops/day:

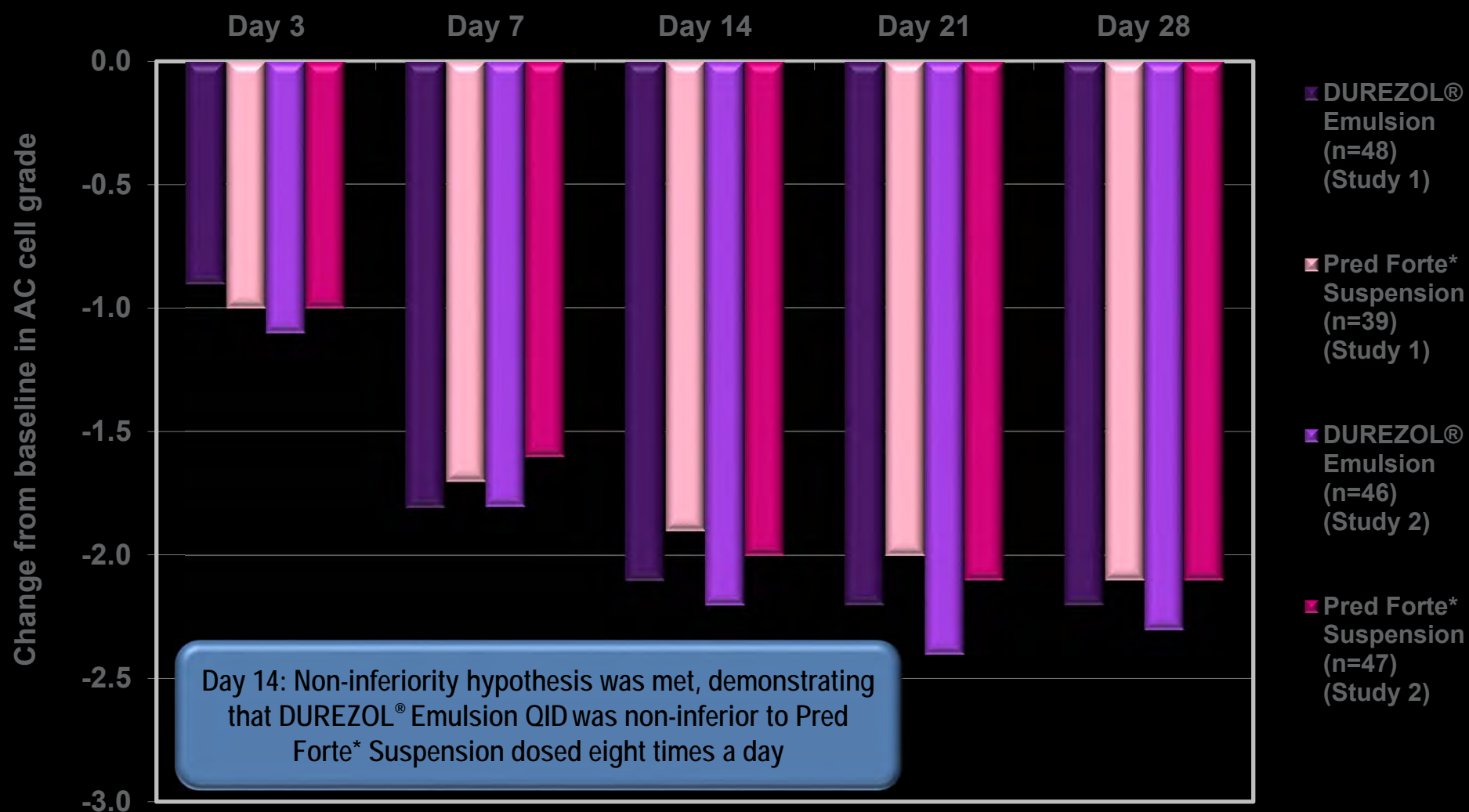
- DUREZOL® Emulsion Group – Bottle A DUREZOL® Emulsion; Bottle B vehicle
- Pred Forte* Suspension Group – Bottle A and Bottle B, Pred Forte* Suspension



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1. Foster CS, Davanzo R, Flynn TE, McLeod K, Vogel R, Crockett RS. DUREZOL® (Difluprednate Ophthalmic Emulsion 0.05%) Compared with PRED FORTE® 1% Ophthalmic Suspension in the Treatment of Endogenous Anterior Uveitis. *J Ocul Pharmacol Ther.* 2010 Oct;26(5):475-83.
2. Data on file, Alcon Laboratories, Inc.

Mean Change from Baseline in Anterior Chamber Cell Grade^{1,2}



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2. Data on file, Alcon Laboratories, Inc.

Treatment-Related Ocular AEs Occurring in $\geq 5\%$ of Patients

Adverse Event	Study 1 ¹		Study 2 ²	
	DUREZOL® Emulsion (n=50) n (%)	Pred Forte* Suspension (n=40) n (%)	DUREZOL® Emulsion (n=56) n (%)	Pred Forte* Suspension (n=54) n (%)
Punctate keratitis	8 (16.0)	5 (12.5)	3 (5.4)	0 (0)
Vision blurred	4 (8.0)	0 (0.0)	1 (1.8)	0 (0)
Iridocyclitis	0	0	5 (5.4)	2 (3.7)
Eye irritation	5 (10.0)	1 (2.5)	1 (1.8)	0 (0)
Dry eye	3 (6.0)	0 (0)	0 (0)	0 (0)
IOP increase ⁺	6 (12.0)	2 (5.0)	5 (8.9)	2 (3.7)

⁺IOP increases that were reported as an AE (which may not have been captured as a "clinically significant IOP rise", or one that was ≥ 21 mmHg and change from baseline ≥ 10 mmHg at the same visit)

According to the full Prescribing Information, the most common adverse reactions reported in the endogenous anterior uveitis studies occurring in 5-10% of subjects included blurred vision, eye irritation, eye pain, headache, increased IOP, iritis, limbal and conjunctival hyperemia, punctate keratitis, and uveitis.³

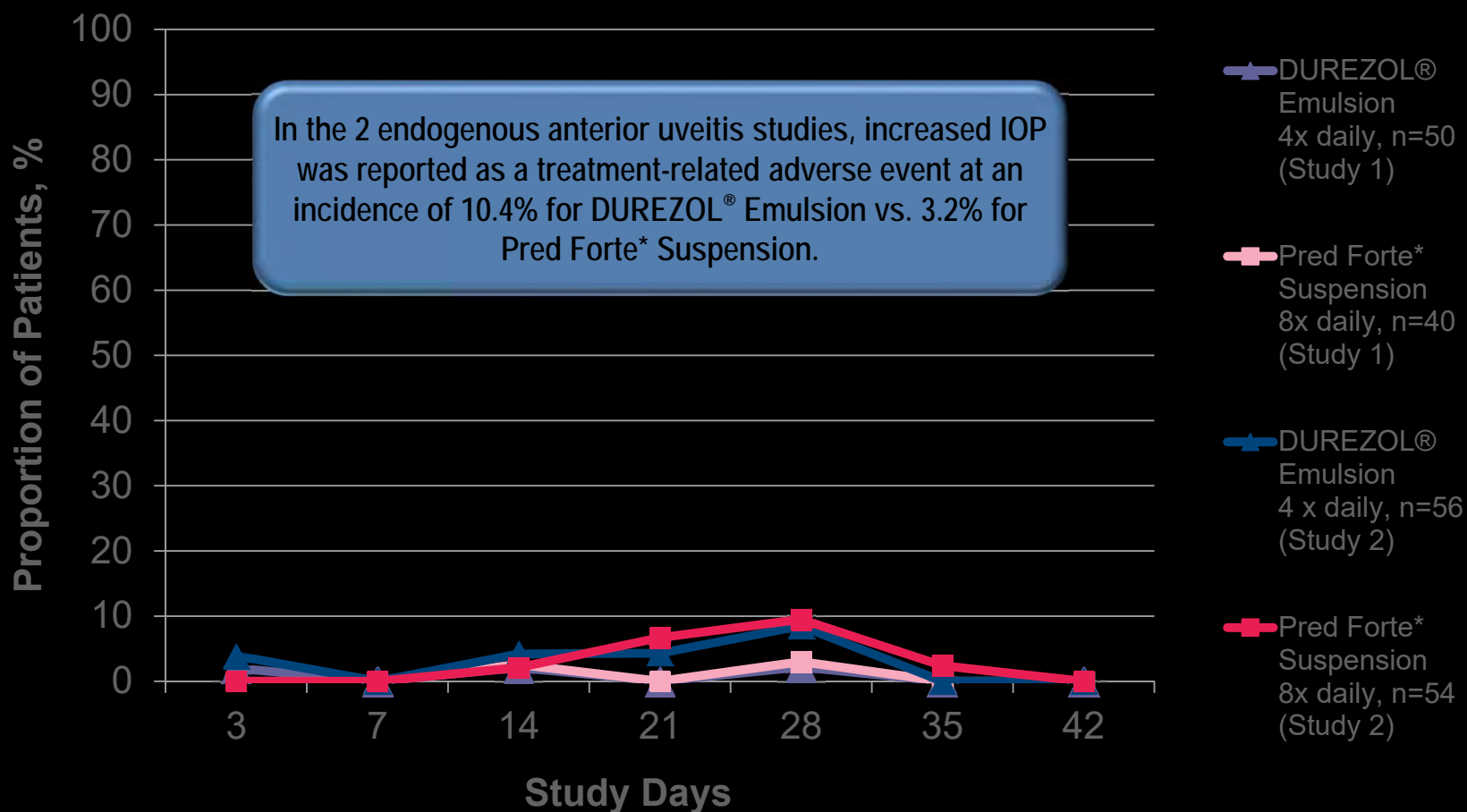
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1. Foster CS, Davanzo R, Flynn TE, McLeod K, Vogel R, Crockett RS. DUREZOL® (Difluprednate Ophthalmic Emulsion 0.05%) Compared with PRED FORTE® 1% Ophthalmic Suspension in the Treatment of Endogenous Anterior Uveitis. *J Ocul Pharmacol Ther.* 2010 Oct;26(5):475-83.
2. Data on file, Alcon Laboratories, Inc.
3. DUREZOL® Emulsion Package Insert

IOP in Endogenous Anterior Uveitis Treatment^{1,2}

Proportion of Patients with Clinically Significant Increases in IOP

Defined as ≥ 10 mmHg increase from baseline and overall pressure of ≥ 21 mmHg at the same study visit



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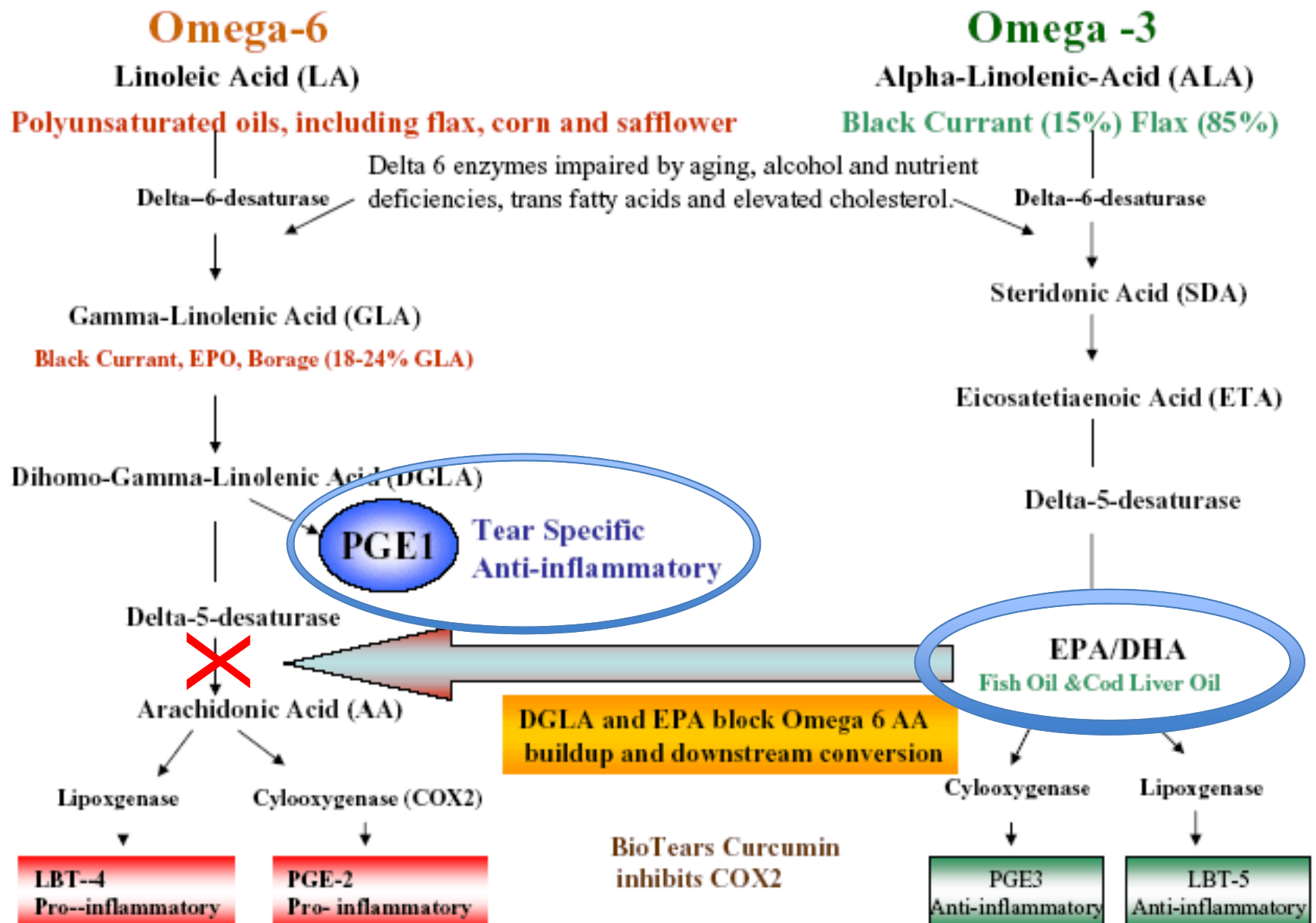
1. Data on file, Alcon Laboratories, Inc.

2. Data on file, Alcon Laboratories, Inc.

Omega - 3's



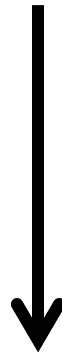
Metabolic Pathways of Omega-3 and Omega-6 Fatty Acids



Why Do Omega 3's Work?



Eicosapentaenoic acid / Docosahexaenoic acid
(EPA/DHA)



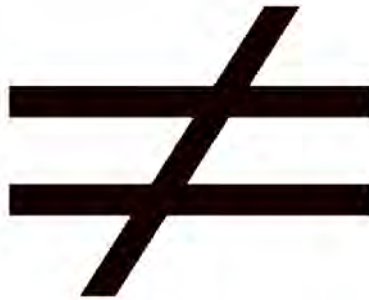
Cyclooxygenase

Prostaglandin - 3
(Anti-inflammatory)

IMPORTANT:



Fish Oil



EPA/DHA

>70%

Tools to Control Pain

- Oral Pain Medications
 - Ibuprofen
 - Norco (formerly Vicodin – Kind of...)
 - Darvocet (recalled)
 - Tylenol 3
 - Tylenol 4

Controlled Substances

- Are placed in schedules
- There are five schedules
- Level of schedule is based on 3 criteria
 - 1) The drugs potential for abuse
 - 2) Does the drug have any medical use?
 - 3) Accepted safety of the drug

Schedule I Controlled Substances

- Highly addictive substances
- Examples:
 - LSD
 - Heroin

Schedule II Controlled Substances

- Highly addictive substances
- Examples:
 - Cocaine
 - Oxycodone (Percocet – acet + Oxycodone)
 - Morphine

Schedule III Controlled Substances

- 1) Lower potential for abuse
- 2) Accepted medical use
- 3) Lower physical dependence
- Examples:
 - Hydrocodone (re-classified as schedule II)
 - Codeine (Note: pure codeine is a CII but codeine with acetaminophen is CIII)

Codeine (3-methylmorphine)

- Is an opiate
- Acts on the central nervous system
 - Brain
 - Spinal cord
- Contain specific opiate receptors
- These receptors play a role in the perception of pain
- Used to produce hydrocodone

Tylenol 3

- Acetaminophen (300 mg) with codeine (30mg)
- Maximum Daily Dosage of acetaminophen not to exceed 4000mg/day
- Maximum dosage of codeine not to exceed 360mg
- 1-2 p.o. q4-6 hrs prn pain

Tylenol 4

- Acetaminophen (300 mg) with codeine (60mg)
- Maximum Daily Dosage not to exceed 4000mg/day
- 1-2 p.o. q6 hrs prn pain

Hydrocodone

- Is an opiate – codeine derivative
- Acts on the central nervous system
 - Brain
 - Spinal cord
- Contain specific opiate receptors
- These receptors play a role in the perception of pain

Vicodin

- Hydrocodone (5 mg), Acetaminophen (500mg)
- Hydrocodone is an opiate derivative of codeine
- Stimulates opiate receptors
- 1-2 p.o. q4-6 hrs prn pain

Norco

- Hydrocodone (5 mg), Acetaminophen (325 mg)
- Hydrocodone is an opiate derivative of codeine
- Stimulates opiate receptors
- 1-2 p.o. q4-6 hrs prn pain

Tramadol

- Commercially available as Ultram
- Schedule IV
- 50mg tablets
- Centrally acting synthetic opioid
- weak inhibition of re-uptake of norepinephrine and serotonin
- Stimulates opiate receptors
- 1 p.o. q6 hrs prn pain

Understanding the Terms

- Analgesic
 - Pain killer or achieving relief from pain
- Antipyretic
 - Reduction of fever
- Anti-inflammatory
 - Reduction of inflammation

Non-Steroidal Anti-inflammatory Drug (NSAID)

- Provides analgesic, antipyretic and anti-inflammatory effects
- Inhibits cyclooxygenase
 - COX-1 and COX-2
 - COX-1 – normal physiological response (stomach)
 - COX-2 – facultatively expressed - inflammation
- COX produces prostaglandins and thromboxanes from arachidonic acid

Ibuprofen

- p.o. q6hrs prn
- 200mg – OTC
- 800mg – prescription



Non-Steroidal Anti-inflammatory Drug (NSAID)

- Contraindicated in patients with known hypersensitivity
- Because of effects on COX, can have gastrointestinal effects on patient
- Rarely can cause autoimmune conditions (stevens johnson syndrome)

Non-Steroidal Anti-inflammatory Drug (NSAID)

- Vioxx (Refecoxib)
 - COX-2 inhibitor
 - Recalled in 2004
 - prescription
- Bextra (recalled)
- Mobic (Meloxicam)
 - 7.5 and 15mg tablets
- Celebrex (Celecoxib)
 - COX -2 inhibitor
 - prescription

Naproxen

- 220 mg p.o. q8-12 hrs prn
- OTC
- 500 mg – prescription strength



Ocular Surface Inflammation

- T-Cells are believed to be the cause of ocular surface inflammation
- Commercially available as Restasis
 - 0.05% concentration
 - Preservative free
 - Single vials
 - Multi-dose bottle
 - Patented non-preserved system that maintains its sterility
- Is an immunosuppressive agent

Restasis (Cyclosporine 0.05%)



Ocular Surface Inflammation

- In patients whose tear production is presumed to be reduced due to ocular inflammation associated with keratoconjunctivitis sicca, cyclosporine emulsion is thought to act as a partial immunomodulatory
- What is the future for cyclosporine
 - Generic formulations may arise

Cequa (cyclosporine 0.09%)

Professional Sample
Not for Sale

NDC 47335-507-97
For topical use in the eye
Sterile, Preservative-Free

 **Cequa™**
(cyclosporine ophthalmic solution) 0.09%

10 SINGLE-USE SAMPLE VIALS
1 pouch x 10 single-use
vials (0.25 mL each)

Rx only
Keep out of reach of children.
Not child resistant.


SUN
PHARMA

Ocular Surface Inflammation

- Intercellular adhesion molecule-1 (ICAM-1) is found on surface cells of the conjunctiva and cornea
- ICAM-1 is overexpressed in dry eye disease
- LFA-1 and ICAM-1 binding is believed to be propagate inflammatory cascade on the ocular surface
 - Is believed to do so by T-cell activation and migration to target tissues

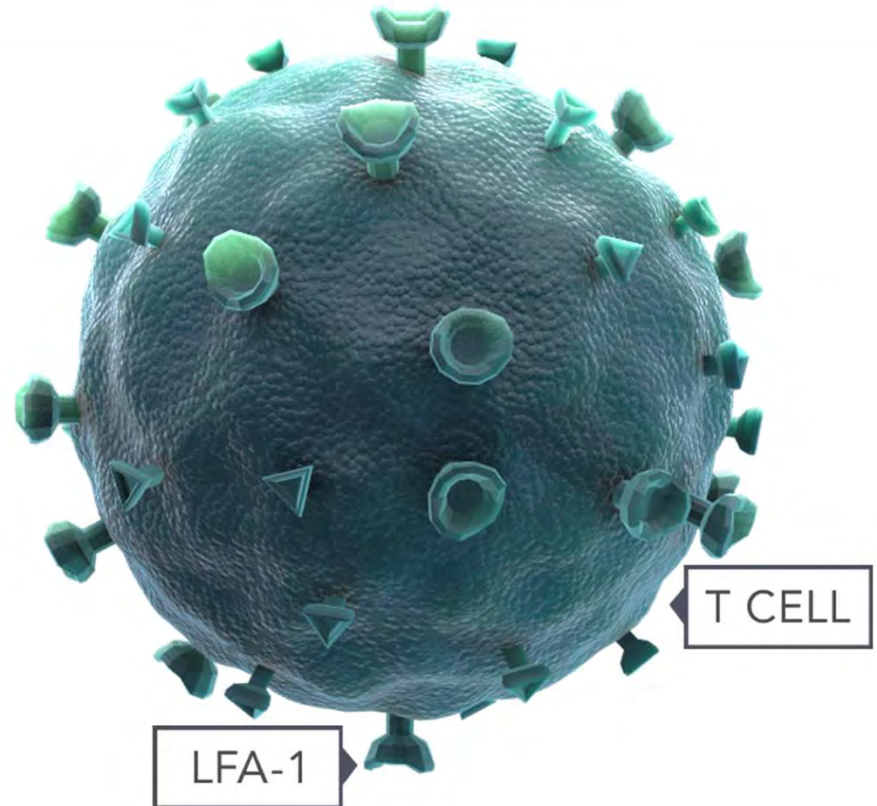
Ocular Surface Inflammation

- Lifitegrast applied topically is believed to prevent the interaction between LFA-1 on T-cells and ICAM-1 on the ocular surface
- Has been shown to improve both signs and symptoms of dry eye within a 12 week time period
- Commercially available as Xiidra
 - 5% concentration
 - non-preserved sterile unit dose vials
- It is a lymphocyte functioning antigen-1 (LFA-1) antagonist



LFA-1 IS AN INTEGRIN RECEPTOR FOUND ON THE SURFACE OF T CELLS^{1,2}

(LFA-1=lymphocyte
function-associated
antigen-1)



DEBS – a unification theory for dry eye and blepharitis

James M Rynerson¹

Henry D Perry²

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²Department of Ophthalmology,
Nassau University Medical Center,
Hofstra University School of
Medicine, East Meadow, NY, USA

Abstract: For many years, blepharitis and dry eye disease have been thought to be two distinct diseases, and evaporative dry eye distinct from aqueous insufficiency. In this treatise, we propose a new way of looking at dry eye, both evaporative and insufficiency, as the natural sequelae of one disease, blepharitis. We suggest the use of a new term in describing this one chronic disease, namely dry eye blepharitis syndrome (DEBS). Bacteria colonize the lid margin within a structure known as a biofilm. The biofilm allows for population densities that initiate quorum-sensing gene activation. These newly activated gene products consist of inflammatory virulence factors, such as exotoxins, cytolytic toxins, and super-antigens, which are then present for the rest of the patient's life. The biofilm never goes away; it only thickens with age, producing increasing quantities of bacterial virulence factors, and thus, increasing inflammation. These virulence factors are likely the culprits that first cause follicular inflammation, then meibomian gland dysfunction, aqueous insufficiency, and finally, after many decades, lid destruction. We suggest that there are four stages of DEBS which correlate with the clinical manifestations of folliculitis, meibomitis, lacrimalitis, and finally lid structure damage evidenced by entropion, ectropion, and floppy eyelid syndrome. When one fully understands the structure and location of the glands within the lid, it becomes easy to understand this staged disease process. The longer a gland can resist the relentless encroachment of the invading biofilm, the longer it can maintain normal function. The stages depend purely on anatomy and years of biofilm presence. Dry eye now becomes a very easy disease to understand. We feel that dry eye should be treated and prevented by early and routine biofilm removal through electromechanical lid margin debridement.

Keywords: biofilm, quorum-sensing gene activation, Demodex, MGD, meibomian gland disease, aqueous insufficiency

Introduction

In 1684, Antonie van Leeuwenhoek presented to the Royal Society of London and commented on the number of “animicules” noted within the scurf of a man's teeth.¹ This is the first known microscopic observation of a biofilm. For over 300 years, little was known about biofilms, and research was uncommon. Biofilm implications in all of human disease were vastly underappreciated.² In the past 20 years, however, biofilm research has burgeoned, with complicated but fascinating interactions between bacteria, host, and their environment now being revealed.^{2,3} In a similar vein, the term “blepharitis” first appears in the literature in the 1800s, but like biofilm research, little progress was made over the subsequent 100+ years in terms of understanding or treating this disease.⁴ While we have made some strides since the days of “Great German Eye Water” to treat “weak or inflamed eyes”, blepharitis remains a poorly defined disease, with the use of confusing and inaccurate terminology and considerable

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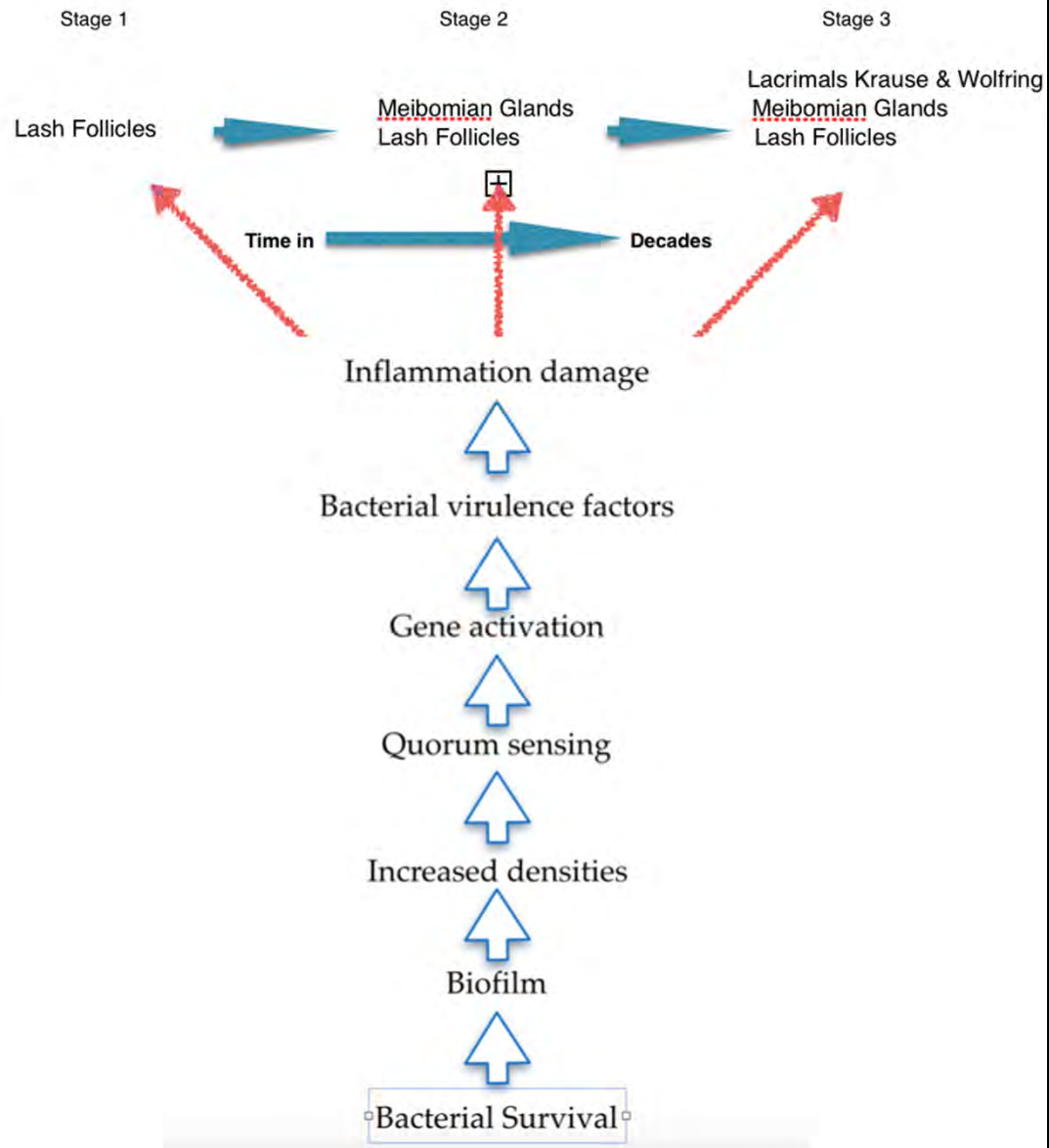
https://doi.org/10.1093/cio/10.1.2455

Clinical Ophthalmology 2016;10:2455–2467

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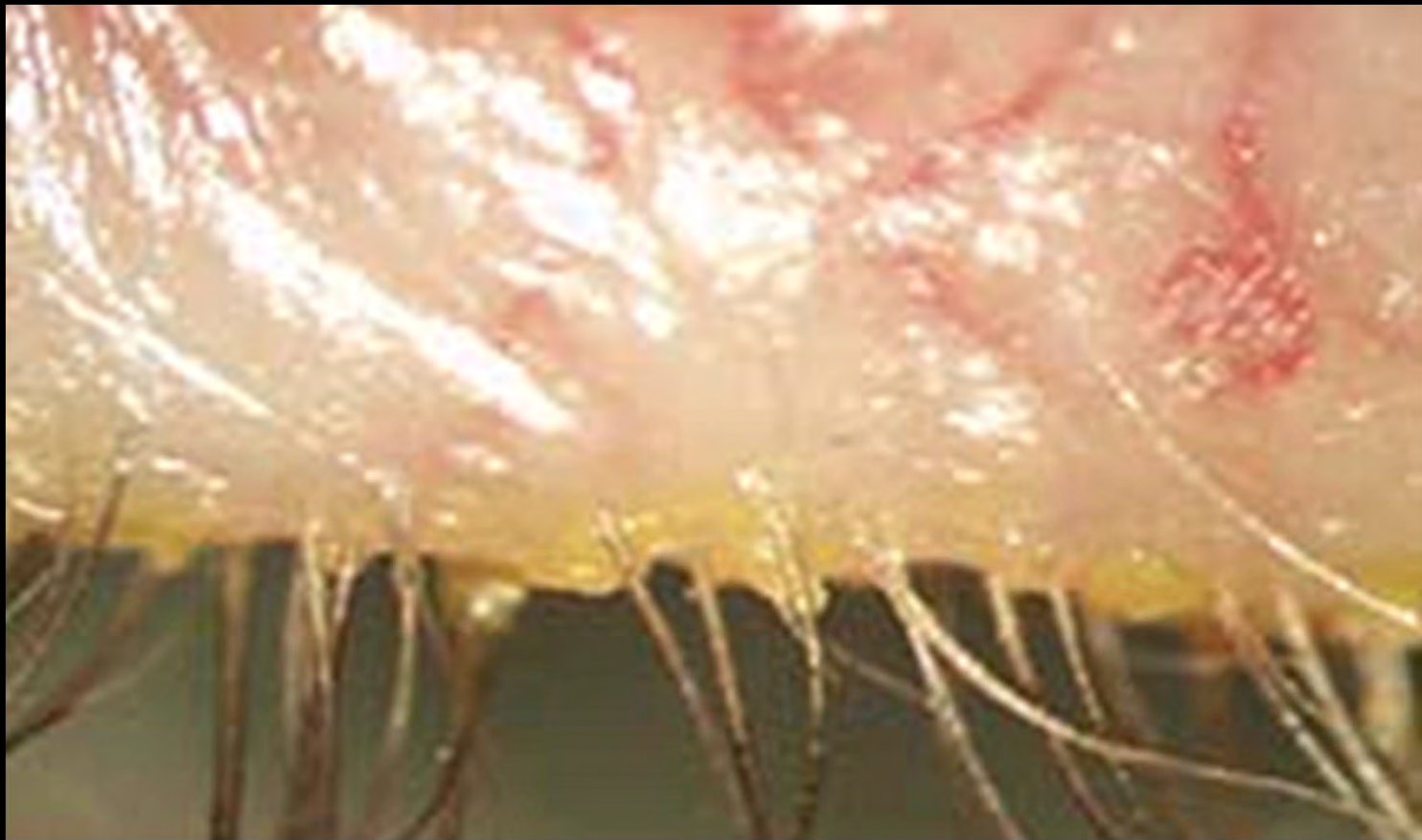
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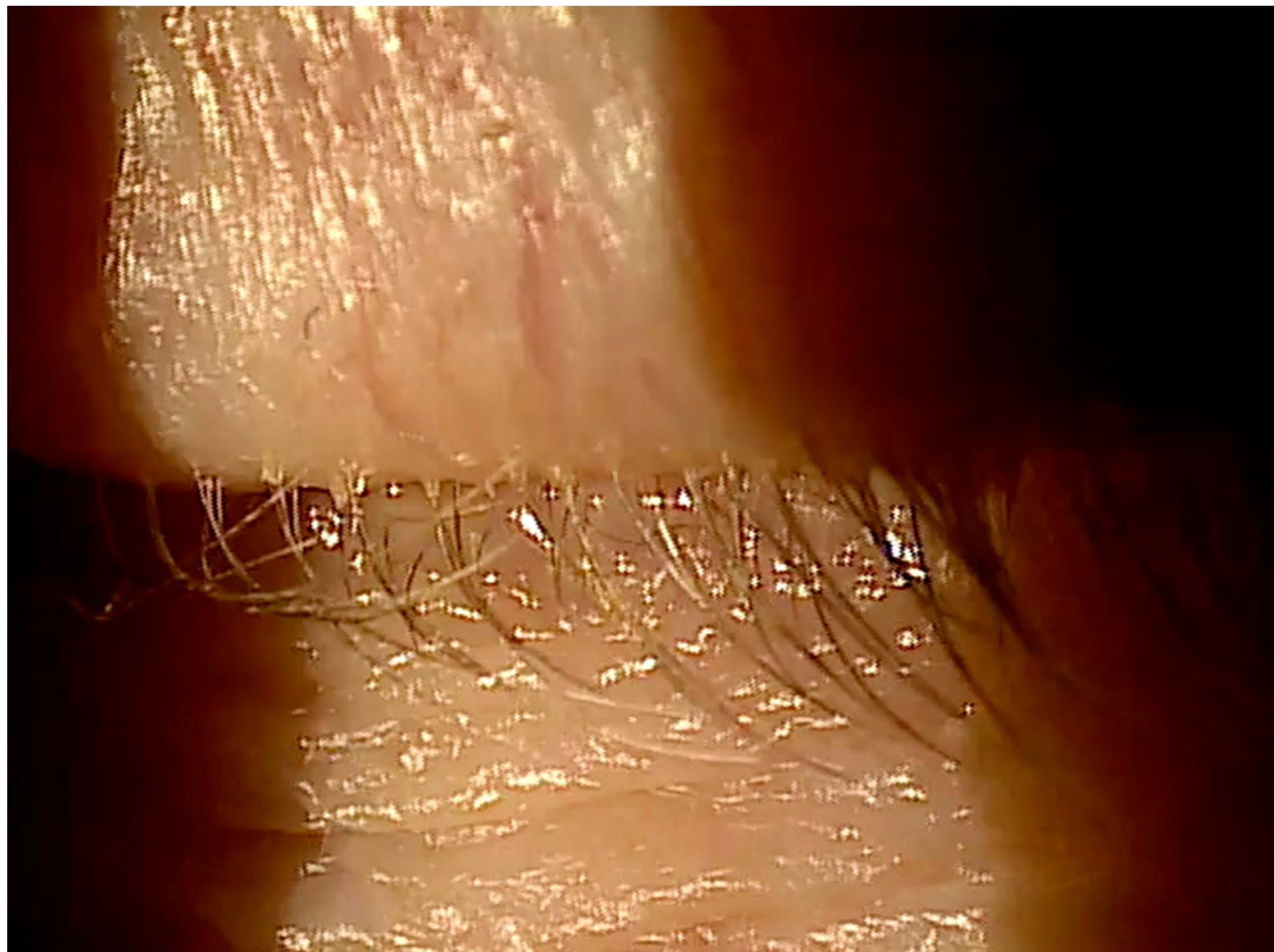
Rynerson Theory of DEBS



Blepharitis

= lid inflammation

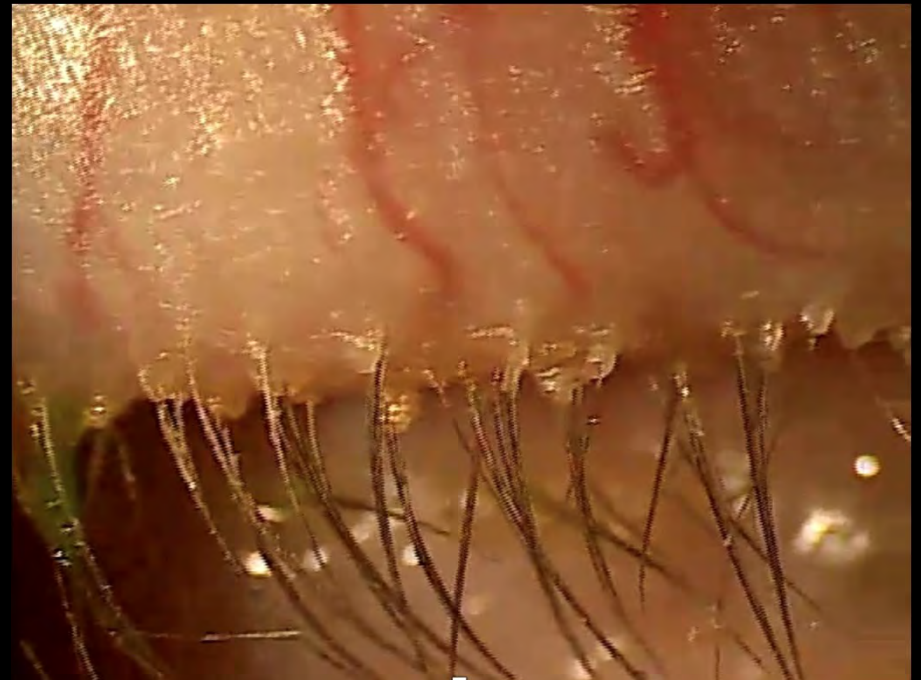




The Problem



Low Mag



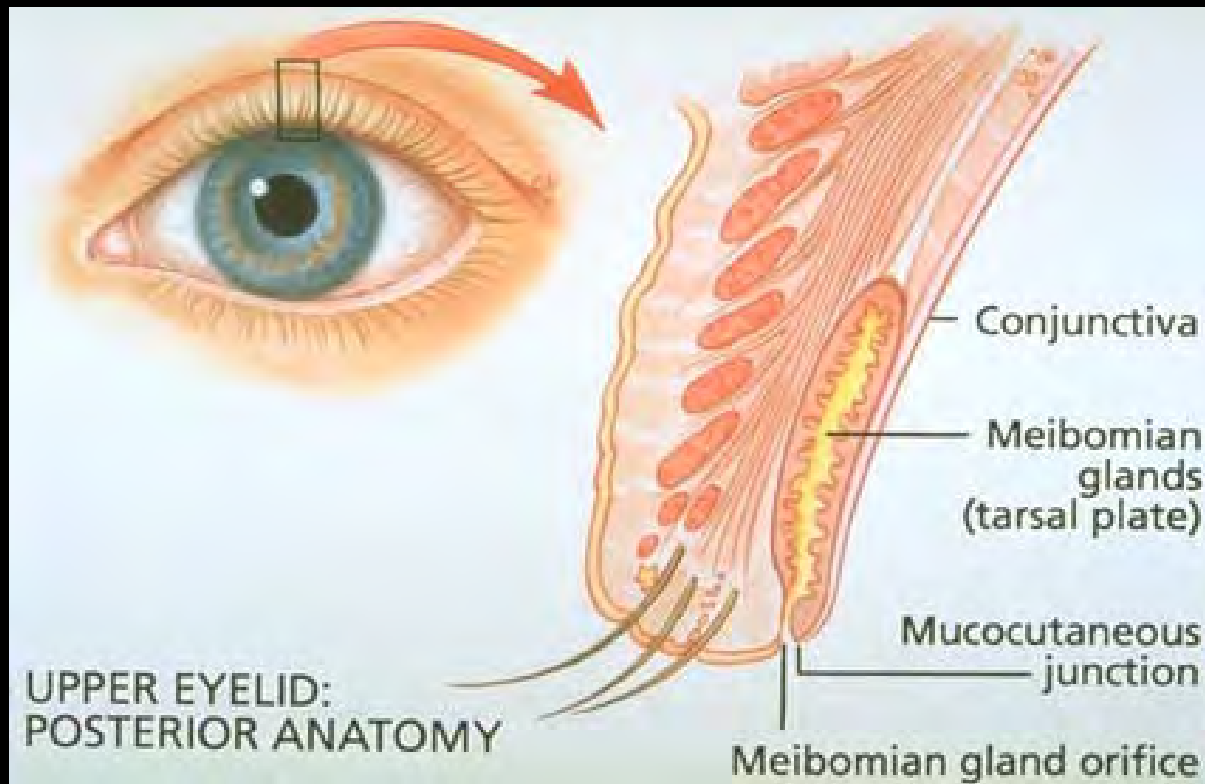
High Mag

The Virulence Factors of Staph aureus

Exoproteins

1. Exotoxins

2. Enzymes - nucleases, proteases, lipases, hyaluronidase, and collagenase



Stages of DEBS

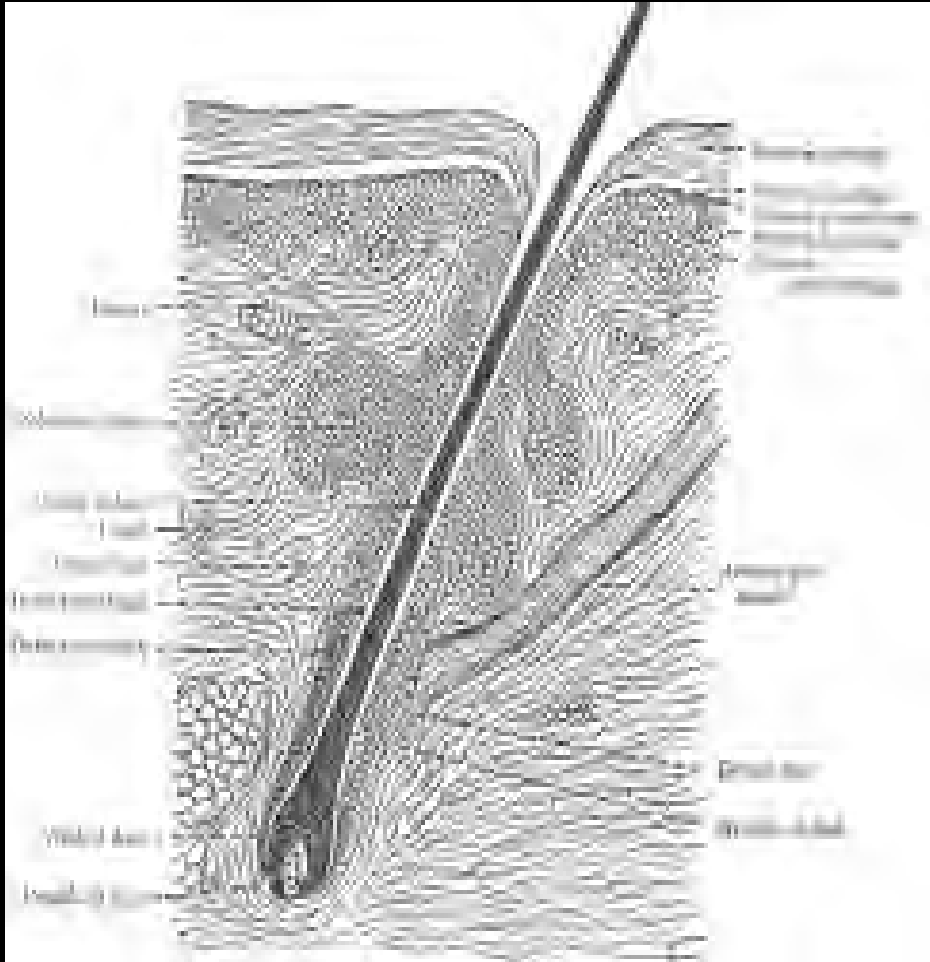
Stage one - folliculitis

Stage two - meibomitis

Stage three - lacrimalitis

Stage four - lid destruction

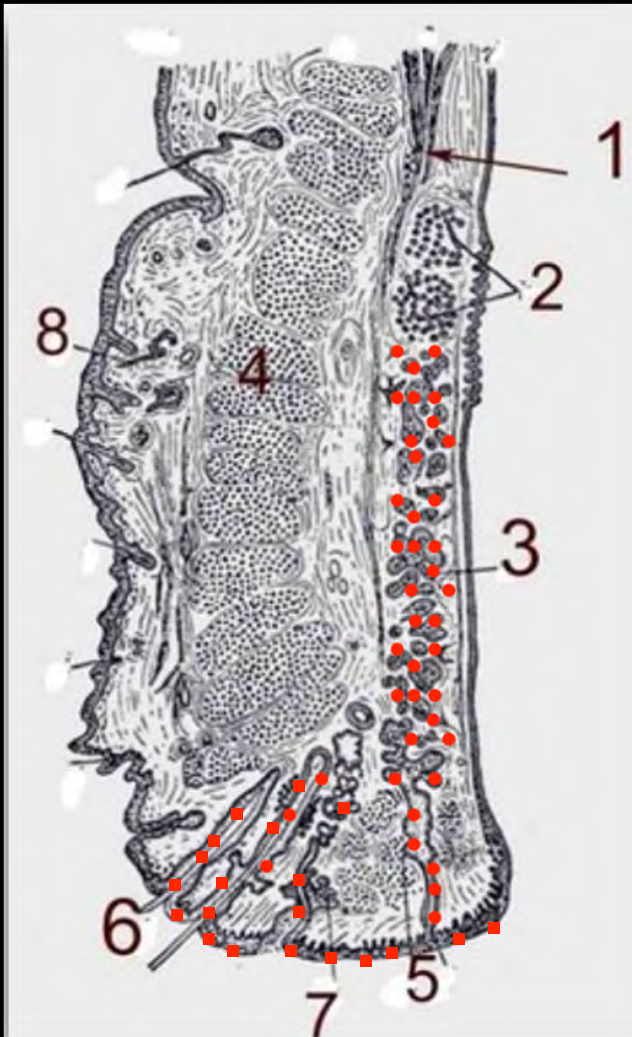
DEBS Stage 1 - Biofilm forms around the lash within follicle



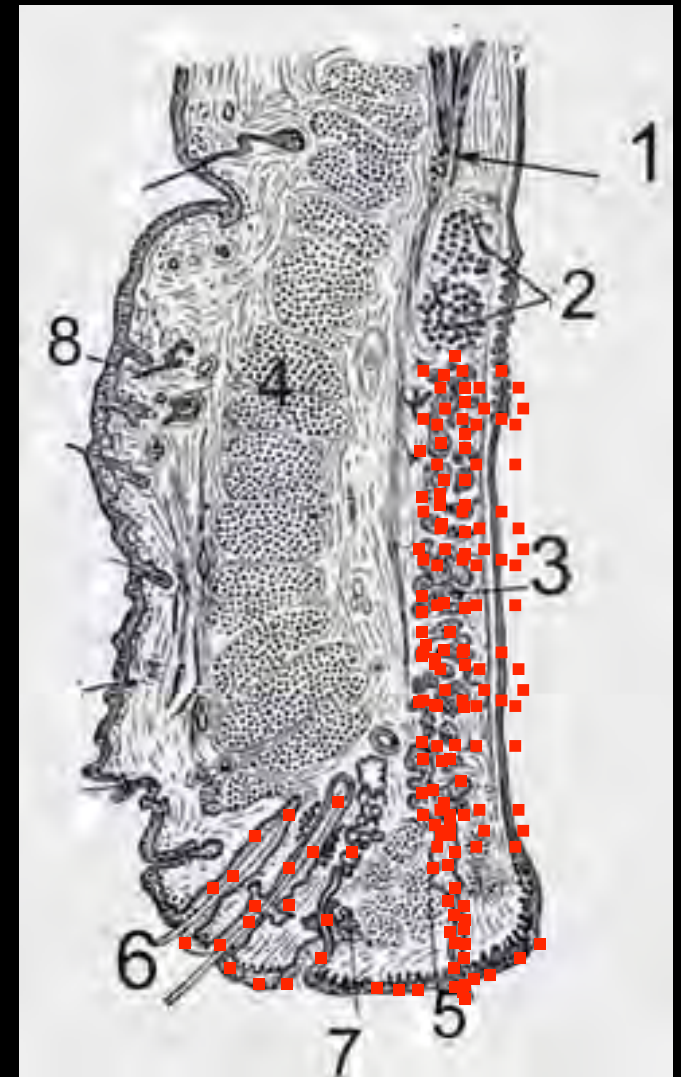
Stage 2 DEBS

MGD

Always occurs
after folliculitis
due to anatomy



Non-obvious MGD



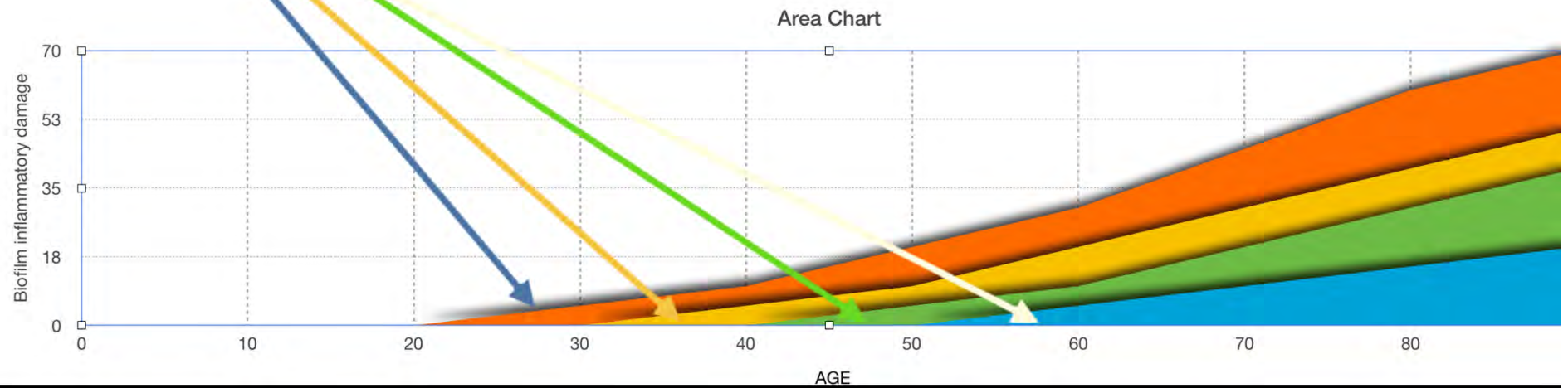
Obvious MGD

MICROBLEPHAROEXFOLIATION (MBE)



Relative Stage of Biofilm Lid Disease per Decade

DESCRIPTION	0	10	20	30	40	50	60	70	80	90
Folliculitis	0	0	0	5	10	20	30	45	60	70
Meibomitis	0	0	0	0	5	10	20	30	40	50
Aqueous insuff	0	0	0	0	0	5	10	20	30	40
Lid destruction	0	0	0	0	0	0	5	10	15	20





Clinical Effectiveness of Lid Debridement with BlephEx Treatment

Daniel Mulder, Kirsti Kyser, Bonnie Rosenberg, Charles Connor, Christopher Choat, Srihari Narayanan

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ABSTRACT

Purpose: Eyelid disease is a common cause of evaporative dry eye. Lid scrubs and warm compresses done consistently will address this problem but poor compliance makes an office based procedure desirable. Korb found the debridement-scaling of the lower lid margin provides statistically significant symptom relief and improvement in the meibomian gland (MG) function. The BlephEx provides a method of accomplishing lid debridement without using a surgical instrument. This study compares signs and symptoms before and after BlephEx treatment.

Methods: Twenty subjects all with MG dysfunction were examined at baseline using a biomicroscope using the Efron scale for grading. Subjects also had a TBUT and OSDI performed. The subjects were then treated with the BlephEx according to manufacturer's directions. 4 weeks later all testing was repeated. Data was analyzed by a t-test with post hoc test for significance.

Results: Subjects TBUT improved from 3.31 ± 1.3 to 5.47 ± 4.3 $p=0.05$. Blepharitis on the Efron scale improved from 1.24 ± 0.69 to 0.575 ± 0.54 $p=0.01$. MG dysfunction also dramatically improved from 1.65 ± 0.5 to 0.76 ± 0.59 $p=0.01$. Symptoms also improved based on the OSDI which went from 43.74 ± 14.27 to 20.33 ± 14.35 $p=0.01$.

Conclusions: This study suggests BlephEx is a viable alternative to lid scrubs and warm compresses. Statistically significant improvement was observed in signs and symptoms of the subjects treated. Eyelid functions improved based on TBUT increase, reduced inflammation and enhanced MG function. Subjects were 50% less symptomatic after treatment. BlephEx appears to be a reasonable clinical approach for use non-compliant MG dysfunction patients.

BACKGROUND

Rynerson introduced a new instrument in 2014 that aims at reducing the effects of blepharitis. The minimal invasiveness of the instrument makes it ideal for use by optometrists.

This study examines changes in the signs and symptoms of the ocular surface before and after treatment with BlephEx.

METHOD

20 subjects with MGD and dry eye symptoms participated in a prospective randomized study.

All subjects underwent an initial baseline examination.

All subjects then received the BlephEx treatment according to the manufacturer's directions.

Outcome measures obtained at baseline and 4 weeks post-treatment included:

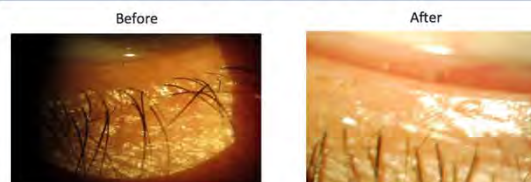
Biomicroscope examination using the Efron Grading Scale to grade MGD and Blepharitis severity

Ocular Surface Disease Index (OSDI)

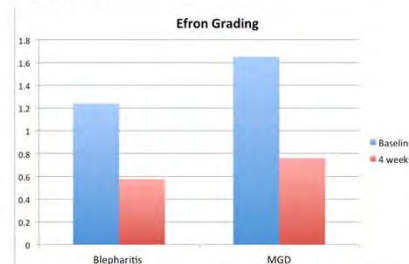
Tear Break-Up Time

Data was analyzed by a t-test with post hoc test for significance.

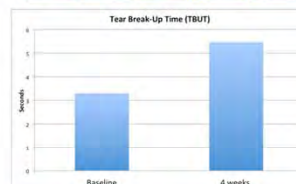
EFRON GRADING SCALE



Inferior lid margin OS; pre-treatment blepharitis rated 2+ (moderate), 4 weeks post-treatment rated 0 (normal).



Efron grading scale for Blepharitis and MGD



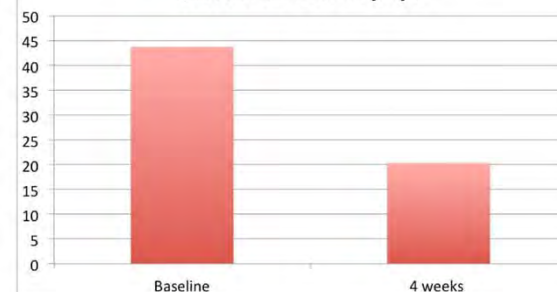
RESULTS

- TBUTs significantly improved 4 weeks after treatment ($p=0.05$)
- Blepharitis on the Efron Scale significantly improved 4 weeks after treatment ($p=0.01$)
- MG Dysfunction drastically improved 4 weeks after treatment ($p=0.01$)
- Symptoms also improved based on the OSDI 4 weeks after treatment ($p=0.01$)

EYELID DEBRIDEMENT



Ocular Surface Disease Index (OSDI) Questionnaire for Dry Eye



CONCLUSIONS

- BlephEx is a viable alternative to the conventional treatment (lid scrubs and warm compresses) for blepharitis
- Statistically significant improvement in signs & symptoms 4 weeks after treatment
- Increased TBUT, decreased inflammation, and increase in MG function after treatment
- Subjects were 50% less symptomatic after treatment

59% of symptomatic CL patients were converted to asymptomatic after just one treatment

Introduction

- 140 million people wear contact lens worldwide and at least 50% of them experience discomfort.
- Comfort is the number one reason why people stop wearing contact lenses.

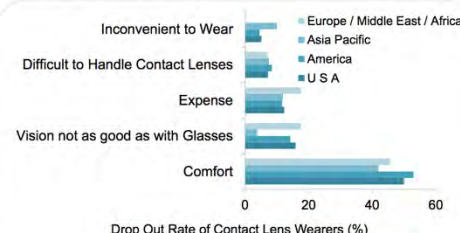
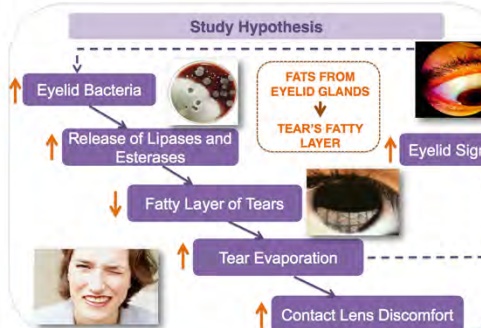


Figure 1: Dropout Rate of Contact Lens Wearers

- No clear consensus on precise reason for development of contact lens discomfort to date.

Purpose

- To evaluate the role of eyelids and tears in contact lens discomfort



Methods



Results

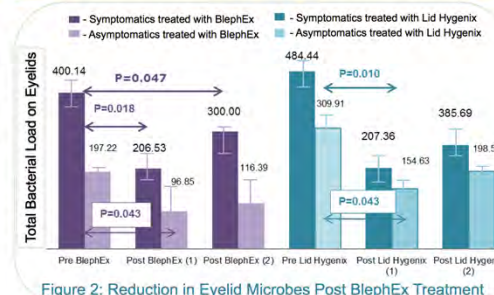


Figure 2: Reduction in Eyelid Microbes Post BlephEx Treatment

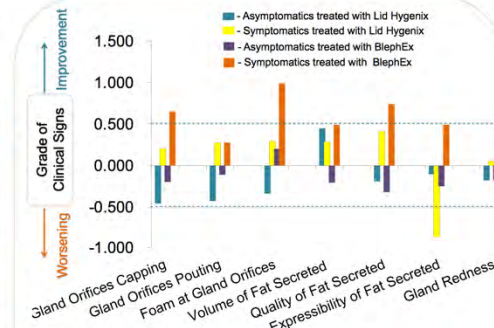


Figure 3: Change in Clinical Grades of Eyelid Glands and Its Secretion Following BlephEx Treatment; $p < 0.05$; Multifactorial Analysis of Variance, Dashed line indicates the level of clinical significance

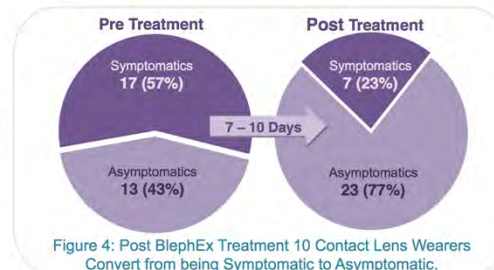


Figure 4: Post BlephEx Treatment 10 Contact Lens Wearers Convert from being Symptomatic to Asymptomatic.

Conclusion

- Symptomatic contact lens wearers had higher number of eyelid bacteria.
- Reduction in eyelid bacteria with BlephEx treatment improved signs of 'fat-producing' eyelid glands and tear's fatty layer; and comfort in symptomatic contact lens wearers.
- 59% of symptomatic lens wearers converted to asymptomatic post BlephEx treatment.

66%
increase
in TBUT
after one
treatment

BlephEx - A Retrospective Analysis of Data Pre and Post Treatment Alice Epitropoulos, MD

177 patients* in total were treated with the BlephEx procedure. Measurements were taken prior to treatment and again at intervals ranging from 1 week to 16 weeks after treatment. Dry eye disease was evaluated using TBUT along with SPEED SCORE, and OSDI questionnaires. Ancillary treatments (artificial tears, etc) were unchanged pre and post treatment.

TBUT was evaluated in 90 patients:

The avg pre-tx TBUT = 5.6 seconds

The avg post-tx TBUT = 9.3 seconds

The results represent a 66% increase in TBUT, with an average follow up time of 3.8 weeks

SPEED score was evaluated in 40 patients:

The avg pre-tx SPEED score = 11.5

The avg post-tx SPEED score = 5.85

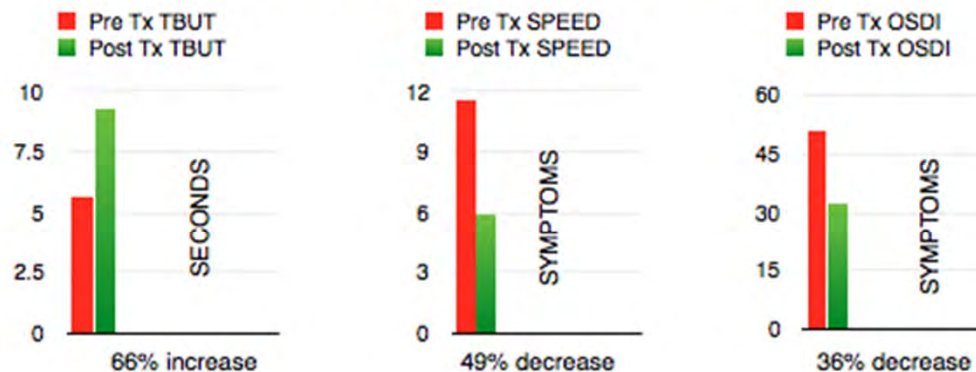
The results represent 49% decrease in SPEED scores, with an average follow up time of 5.4 weeks

OSDI score was evaluated in 15 patients:

The avg pre-tx OSDI score = 50.60

The avg post-tx OSDI = 32.3

The results represent a 36% decrease in OSDI scores, with an average follow time of 3.8 weeks

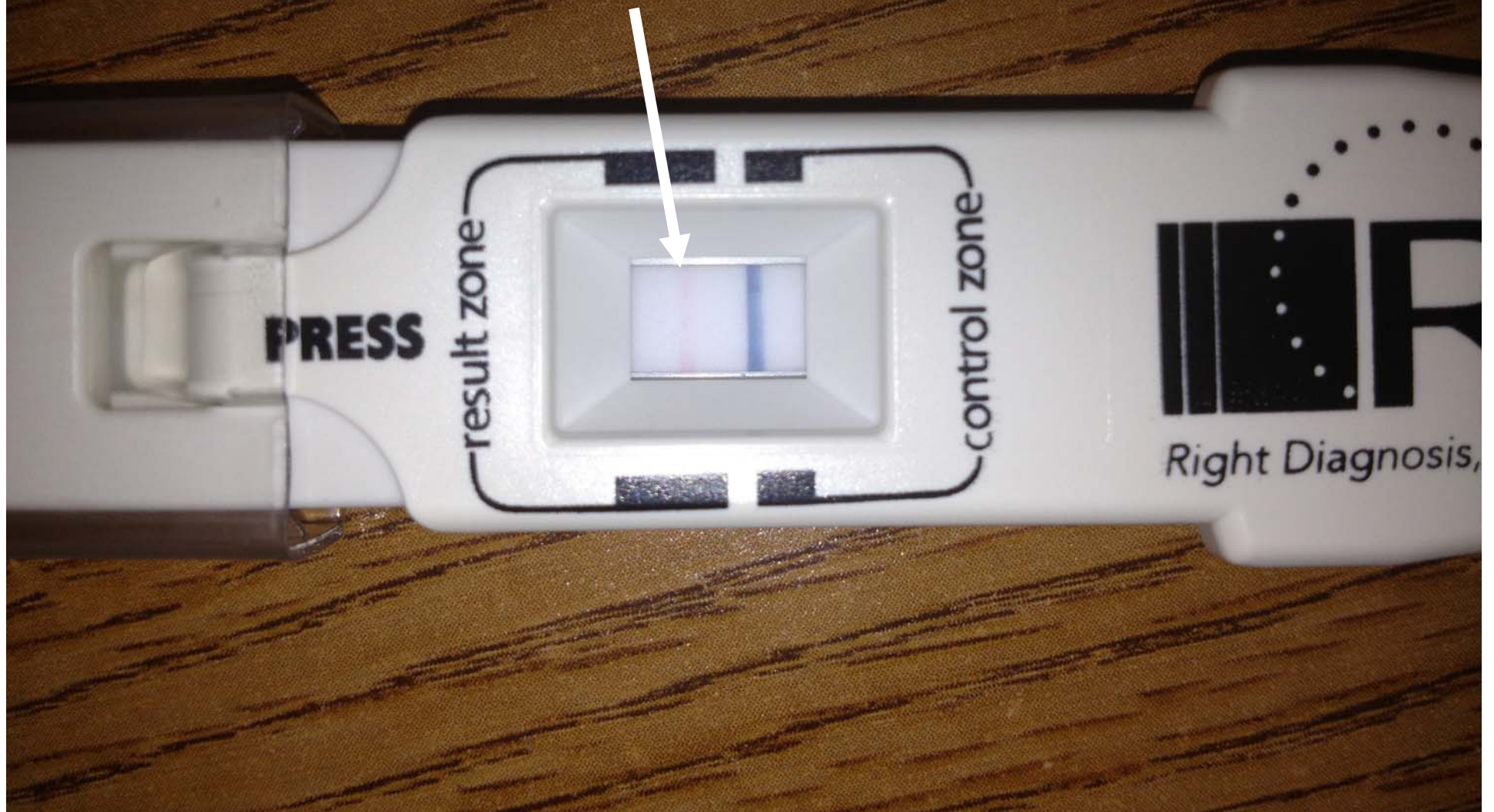


The results of this analysis closely mimic a previous study on 20 MGD patients performed by Mulder, et al, in 2014, in which the results included TBUT and OSDI. They found that after 4 weeks of follow up, TBUT increased by 65% and OSDI decreased by 53.5%. While not a prospective, controlled study, these consistent results should compel us to re-evaluate how we are currently treating our dry eye patients, and seriously consider adding the biofilm-removing BlephEx to our standard dry eye treatment protocol.

*Practices submitting data for this analysis were: Michiana Eye Center, Dr. Oliver, Midway Optometry, Dr. Gregory Hayden, Dr. Anil Sethi, Florida Eye Specialists, Dr. Fikret Kajoshaj, Dr. Kyle Ross, Dr. Tauseef U. Tahir, Dr. Eric Schmidt, Dr. Debra Kolems, Dr. Alice Epitropoulos, Dr. Richard Kootman, Dr. Lisa Ely, Dr. Srihari Narayanan, Dr. Stéphane Laframboise, Orlando Eye Institute, Virginia Eye Center, Dr. Scott Schachter, Eye Institute Of South Jersey, Dr. Charles Clayton, Dr. Susan Watson, Dr. Lisa Chriss, Focus Eyecare Centre, Dr. Doug Devries, Dr. Shalu P.A., Dr. Steven DeGroff, Bundy Premier Eye Center, Collins Vision, Dr. Helen Boerman, Dr. Kevin Gee, Vision Source Willowbrook



This can vary in signal strength





8 ng/mL
Negative

34 ng/mL
Trace Positive

66 ng/mL
Weak Positive

101 ng/mL
Positive

381 ng/mL
Strong Positive

OPEN ACCESS


ARVO Annual Meeting Abstract | June 2017

Reduction in inflammatory marker matrix metalloproteinase-9 following lid debridement with BlephEx

[Charles G Connor](#); [Srihari Narayanan](#); [William Miller](#)

+ Author Affiliations & Notes

Investigative Ophthalmology & Visual Science June 2017, Vol.58, 498. doi:

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 TOOLS ▼

Abstract

Purpose : Meibomian Gland Disease (MGD) is a common cause of evaporative dry eye. Lid scrubs and warm compresses can address this problem but poor compliance makes an office based procedure desirable. Korb found the debridement-scaling of the lower lid margin provides statistically significant symptom relief and improvement in MG function. The BlephEx provides a method of accomplishing lid debridement without using a surgical instrument. Ocular surface inflammation is well documented in dry eye patients. The RPS InflammDry recognizes elevated levels of MMP-9, an inflammatory marker that is consistently

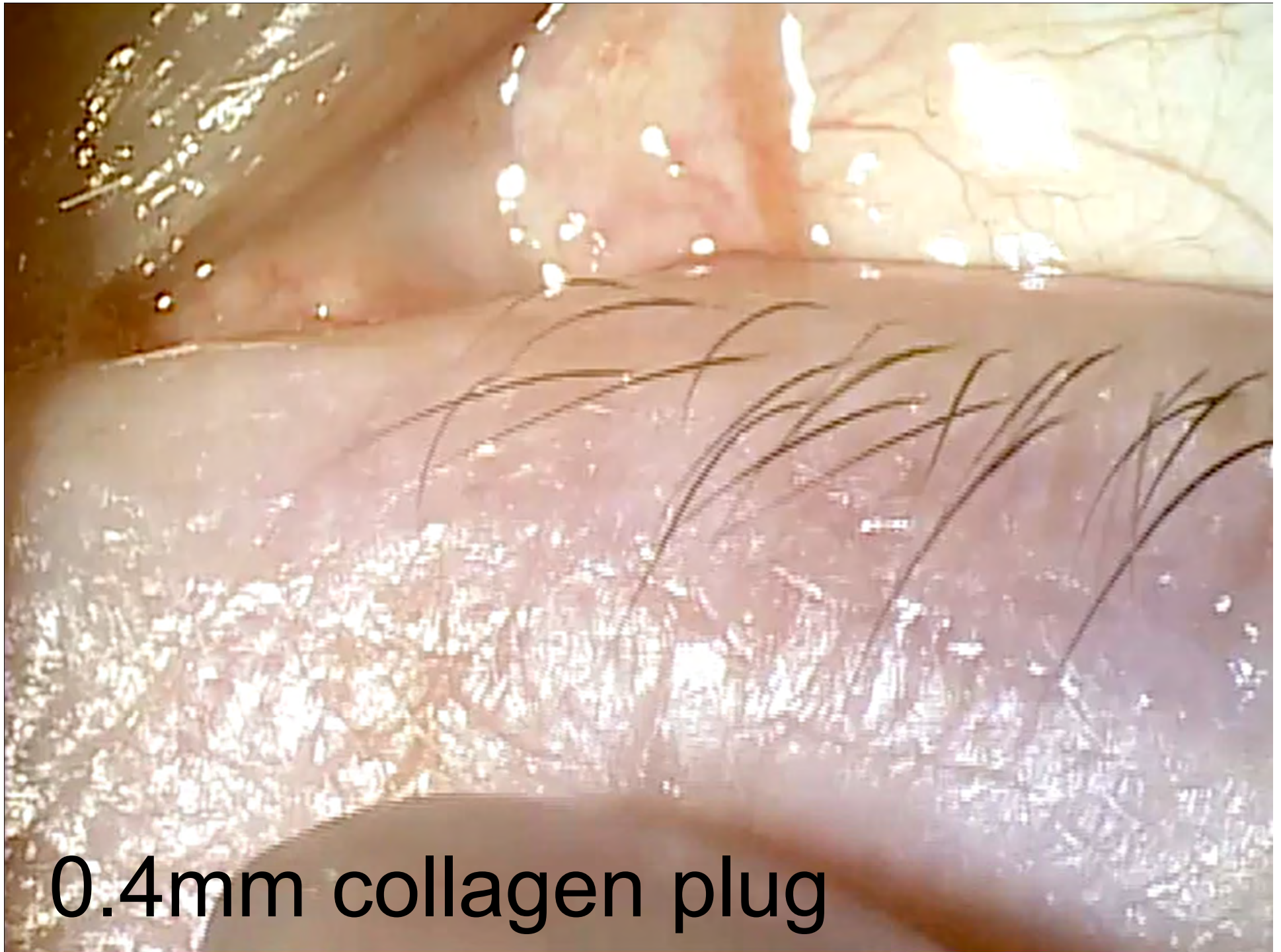
- Ten MGD patients with evaporative dry eye and tested positive with InflammDry
- OSDI, NIBUT, meibography and InflammDry were measured before and after BlephEx treatment (4 week post treatment)
- OSDI – 26 (pre-treat) and 10.66 (post-treat)
- NIBUT – 6.99 (pre-treat) and 9.53 (post-treat)
- Meibography – no change
- InflammDry – positive (pre-treat) and negative (post-treat)

Punctal Occlusion



Jewelers Forceps





0.4mm collagen plug



0.2mm 3 month plug

Punctal Plugs

Permanent

Pedi-Plug
X-Small
Small
Medium
Large
X-Large

Temporary

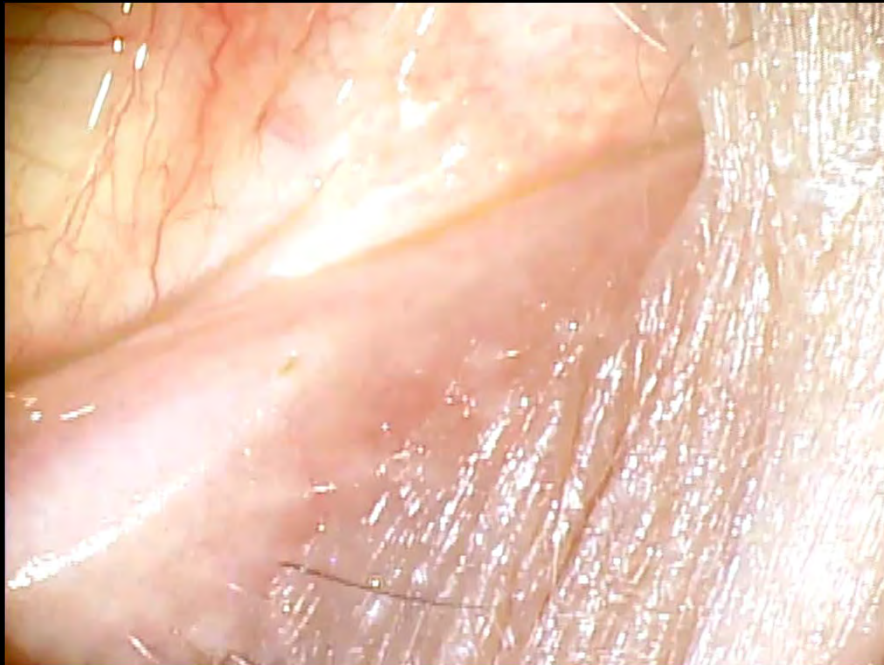
Collagen
(10-14 days) { 0.2 mm
0.3 mm
0.4 mm

3 month { 0.2 mm
0.3 mm
0.4 mm
0.5 mm

6 month { 0.3 mm
0.4 mm
0.5 mm

Recently
Became
Available

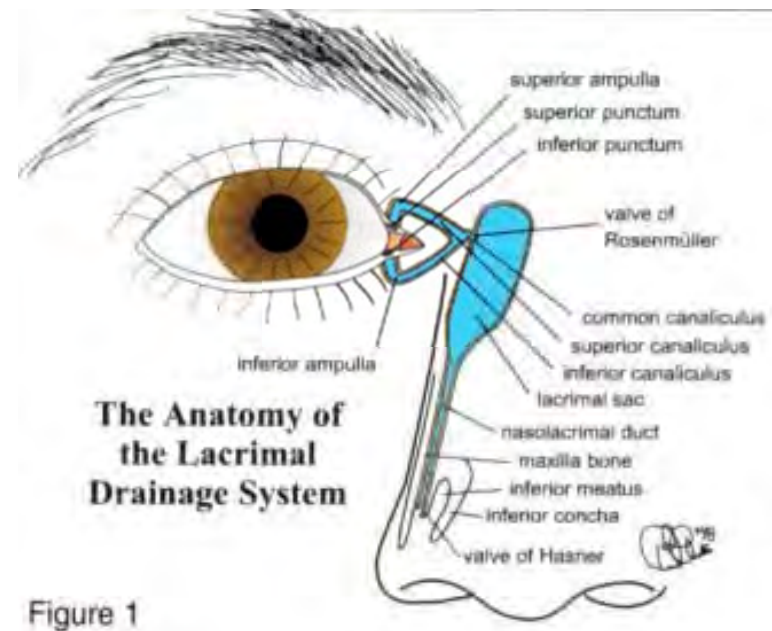
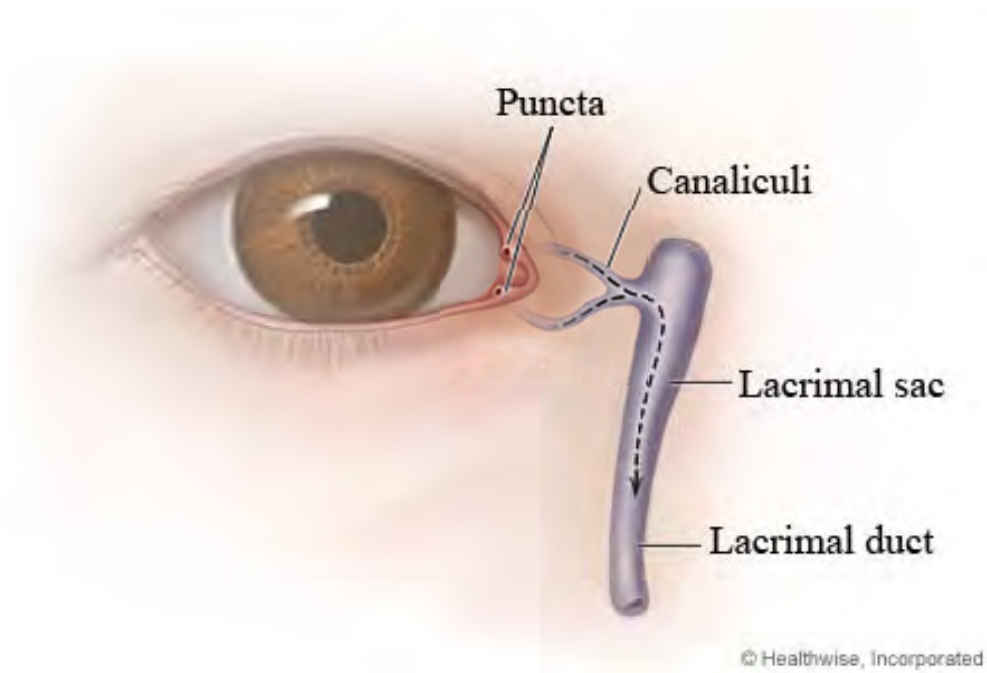
Various Size Puncta



0.2 mm 3 month

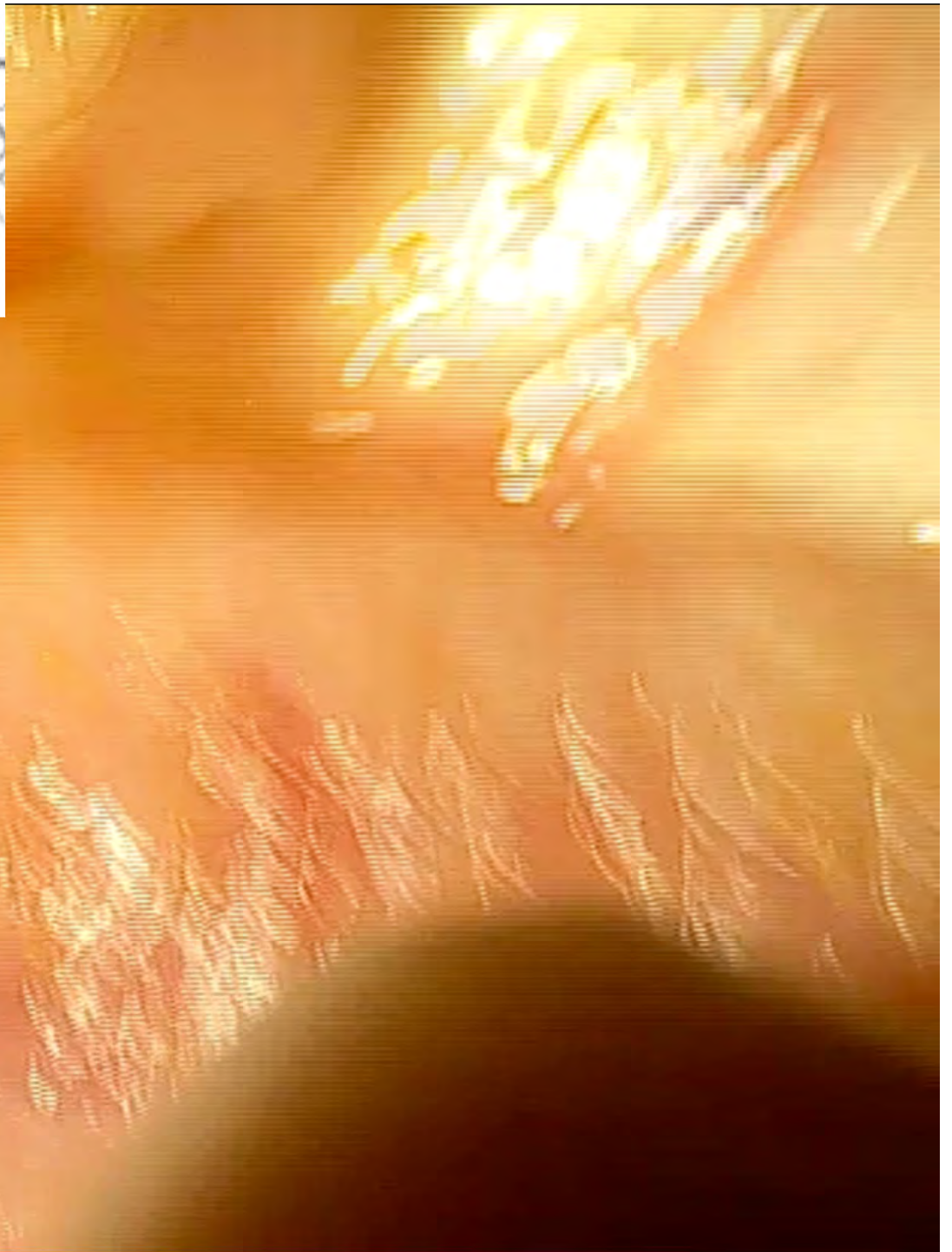
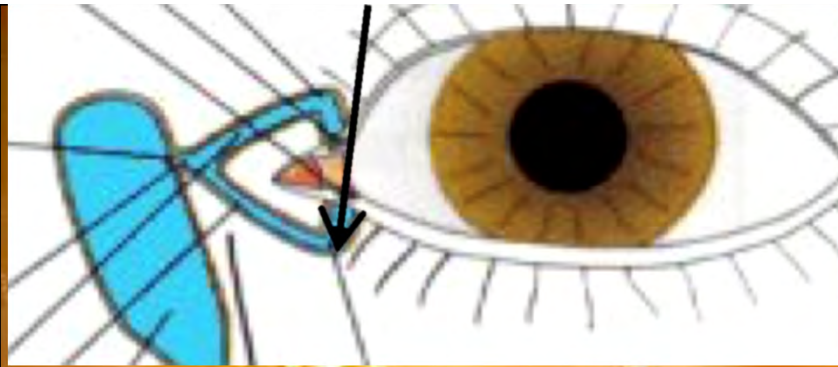


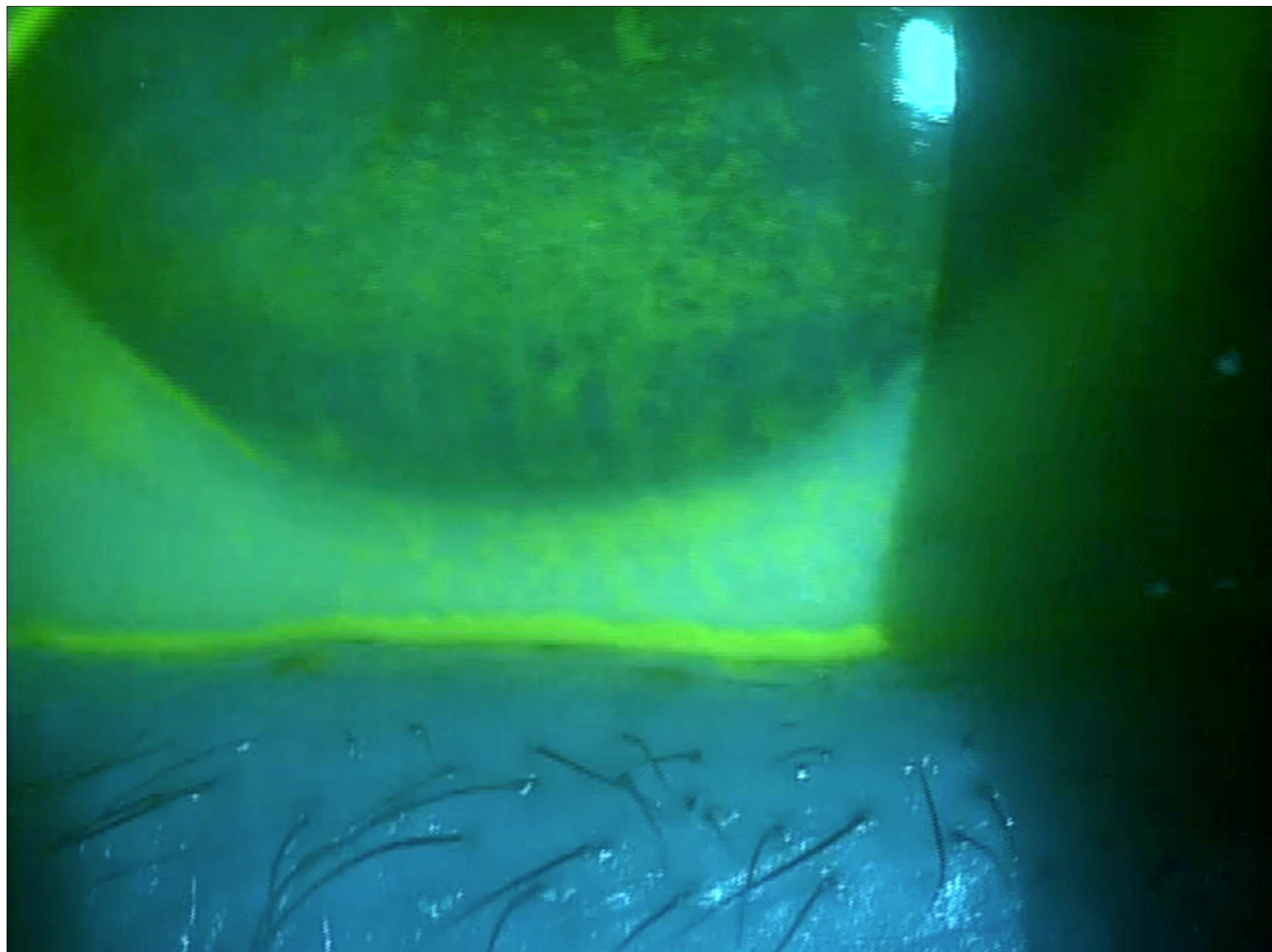
0.4 mm collagen



<http://www.academy.org.uk/tutorials/dilate1.jpg>

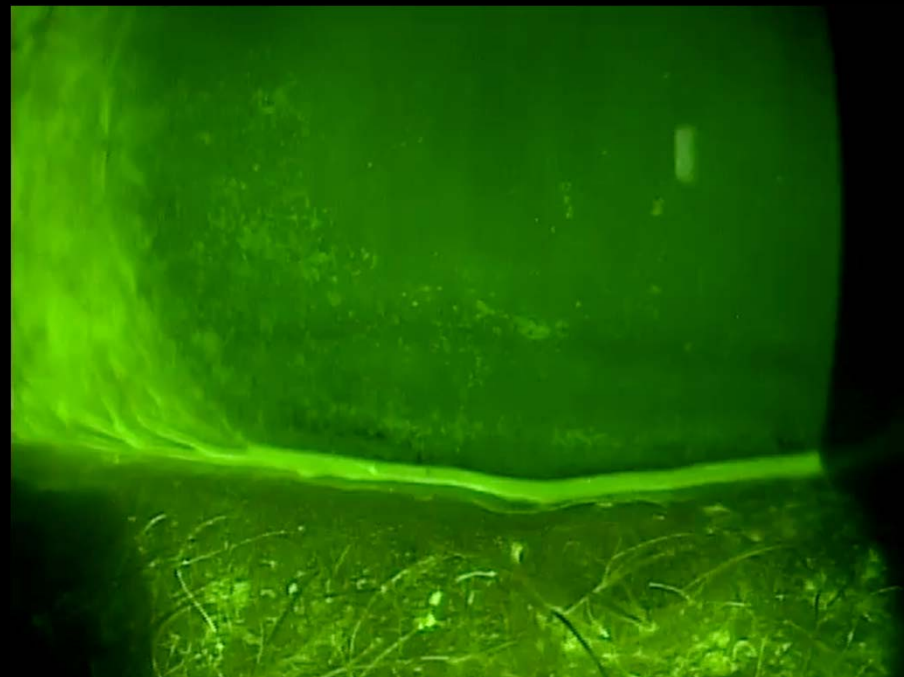
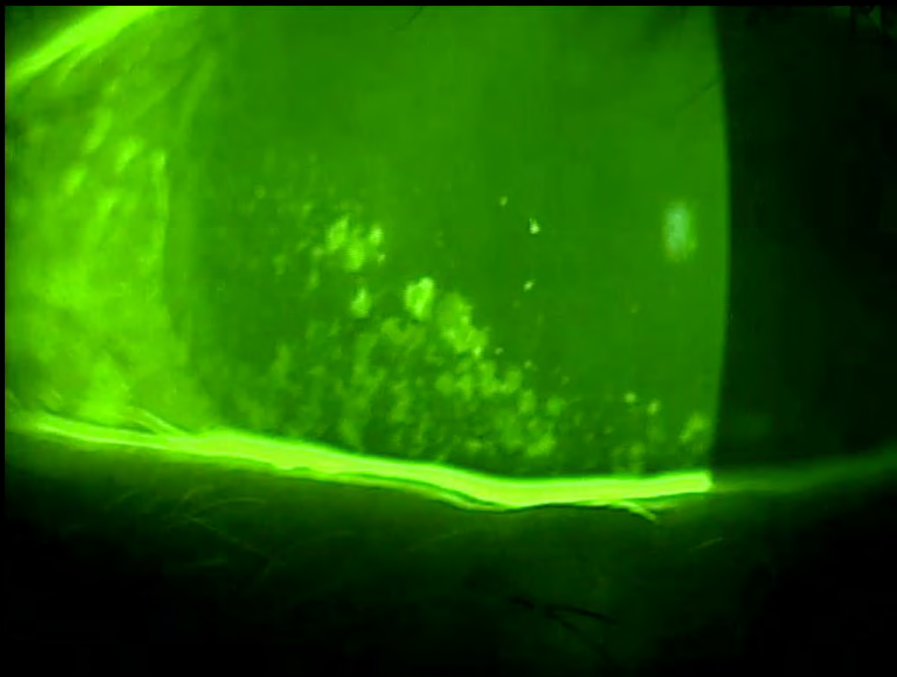
http://www.uofmhealth.org/sites/default/files/healthwise/media/medical/hw/h9991911_001.jpg



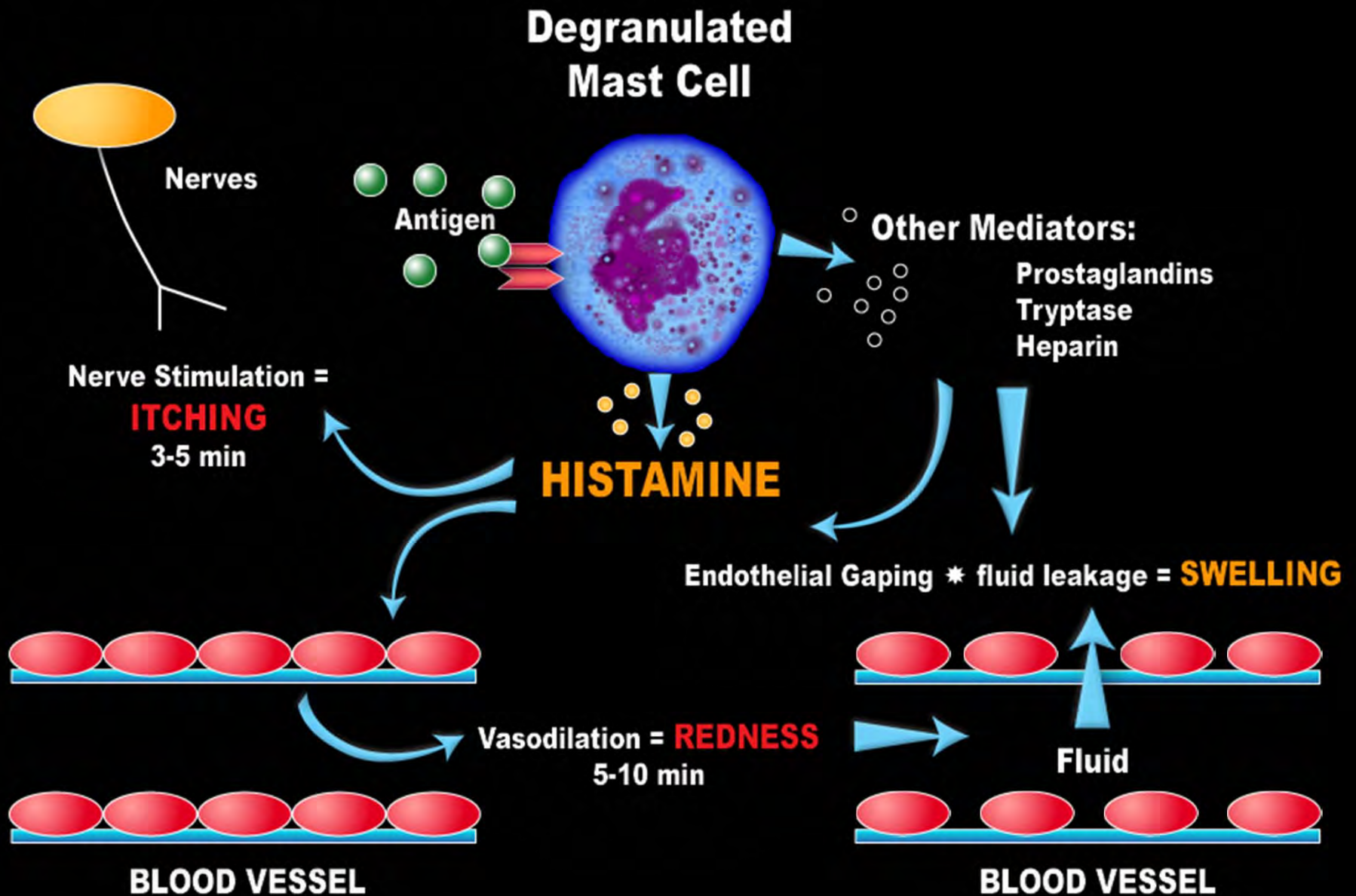


Before Plugs

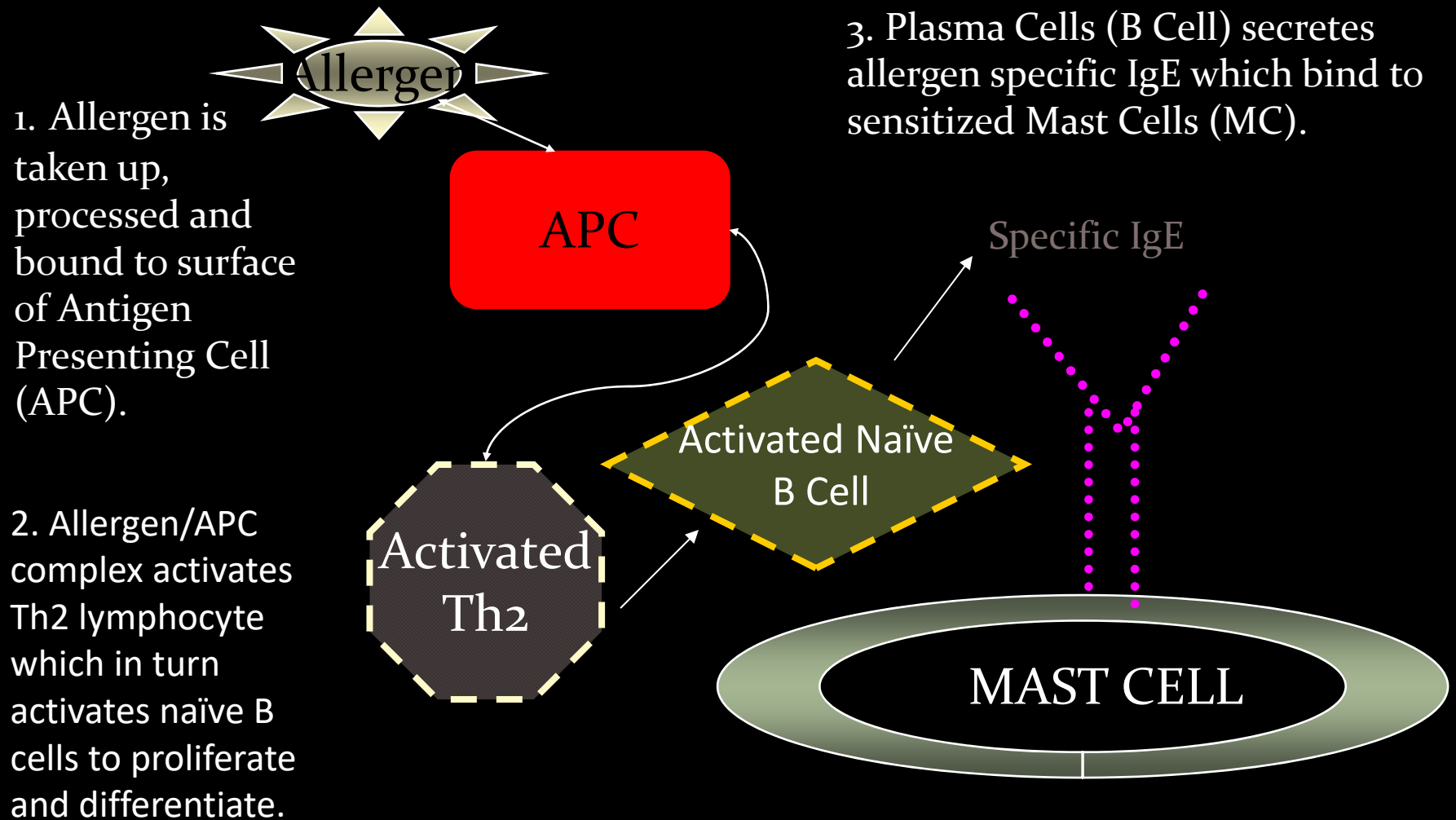
2 weeks



The Allergic Cascade



Allergic Response

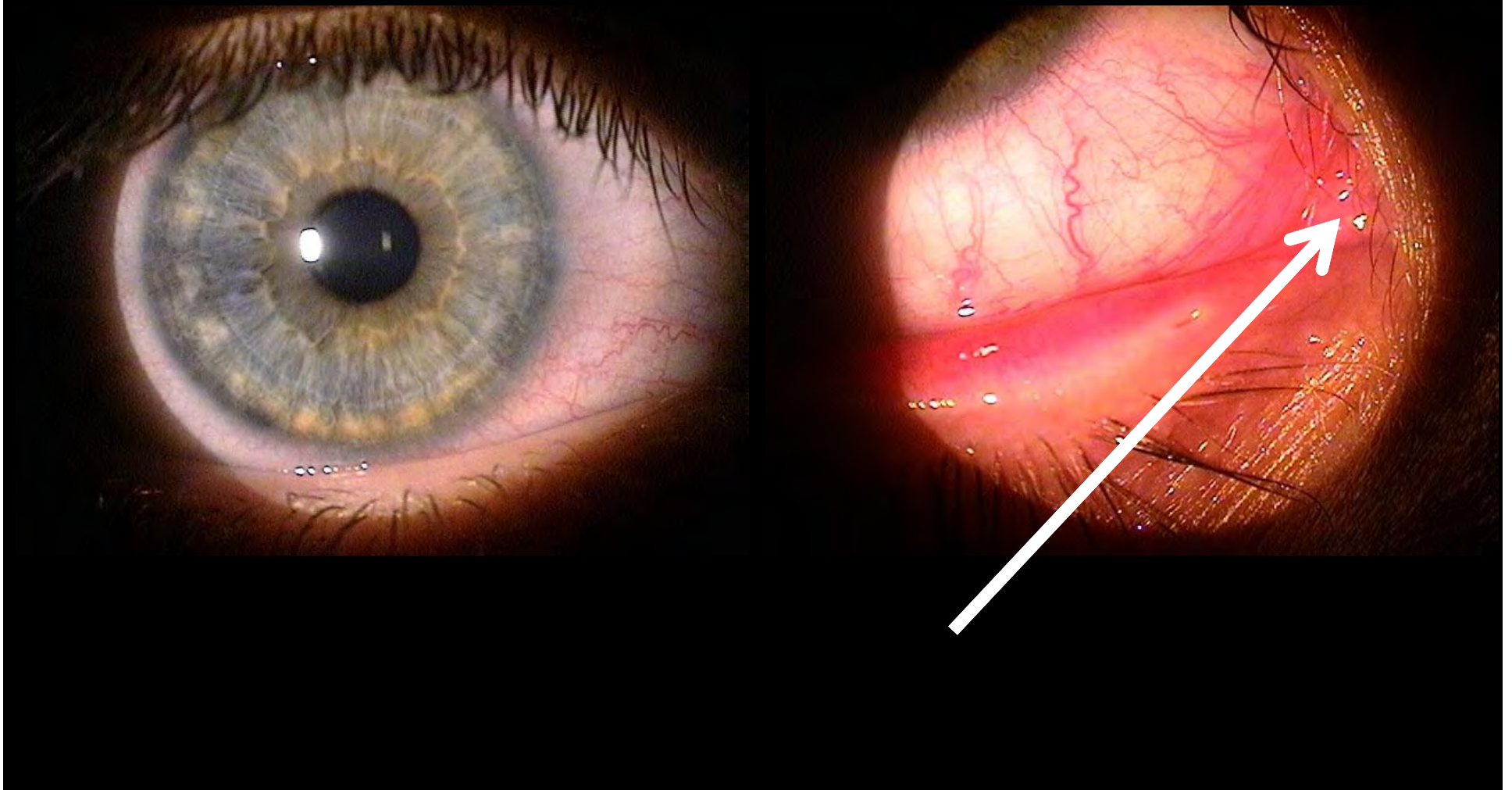


Thank you to Dr. Gil Pierce

Types of Allergic Eye Disease

- Acute allergic conditions
 - Seasonal Allergic Conjunctivitis (Hay Fever) - SAC**
 - Perennial Allergic Conjunctivitis – PAC**
- Chronic allergic conditions
 - Vernal Conjunctivitis - VKC**
 - Atopic Conjunctivitis - AKC**
 - Giant Papillary Conjunctivitis - GPC**

Misunderstanding the Itchy Eye



Allergic Conjunctivitis: Seasonal / Perennial

Causes:

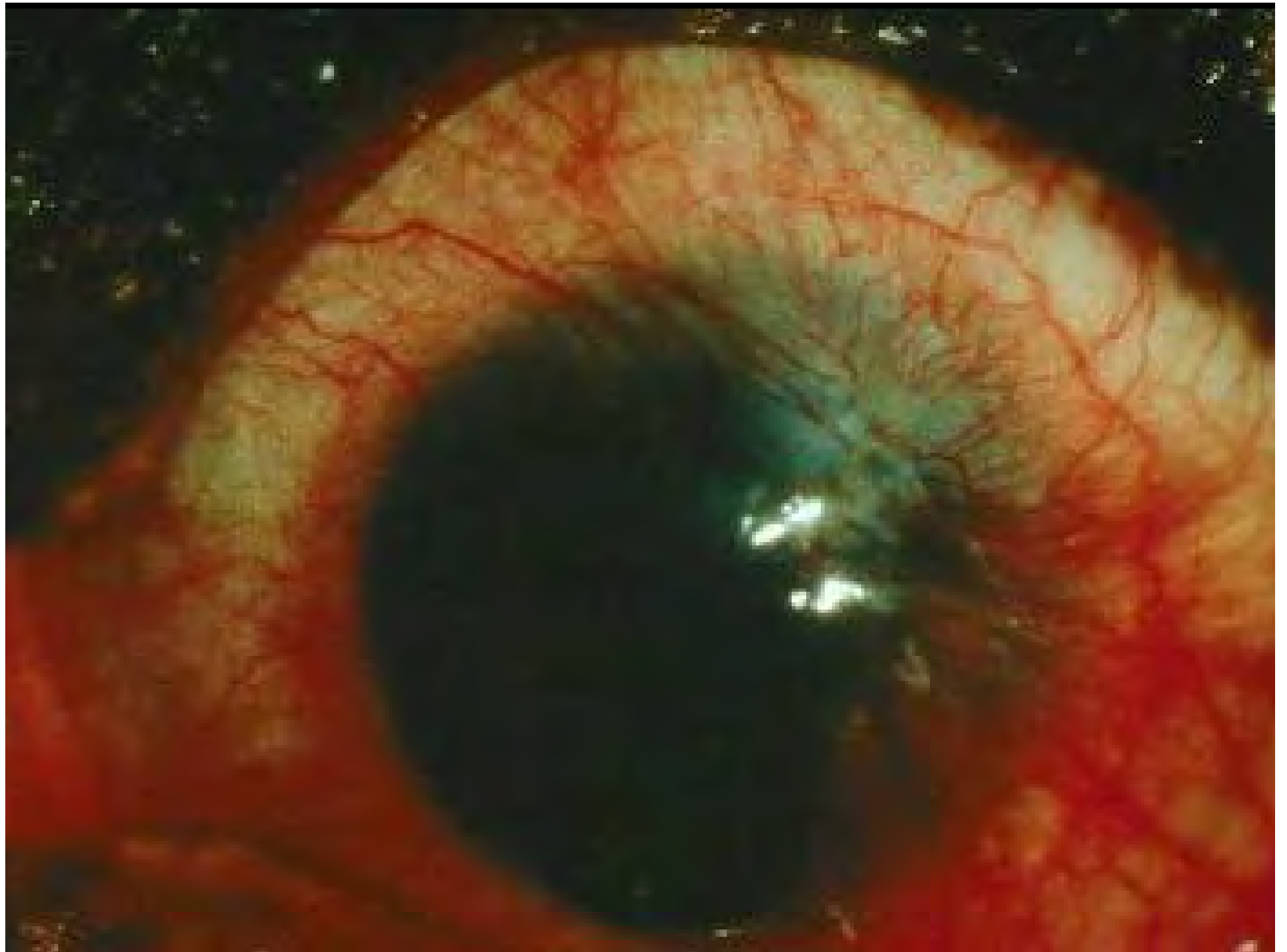
Environmental
Genetic predisposition

Findings:

Family history
No eosinophils found in scrapings
Spike in tear histamine
Normal histaminase function

Signs/Symptoms:

Itching
Redness
Chemosis
Lid swelling
Tearing



Atopic Keratoconjunctivitis (AKC)

Causes:

Associated with atopic dermatitis

May be perennial

Genetic predisposition

Environmental antigens

Clinical Findings:

Initiates between 20 and 50 years of age

Elevated levels of eosinophils, TH₂, lymphocytes, and mast cells

Signs/Symptoms:

Itching

Redness

Photophobia

Keratopathy

SPK/Ulcers

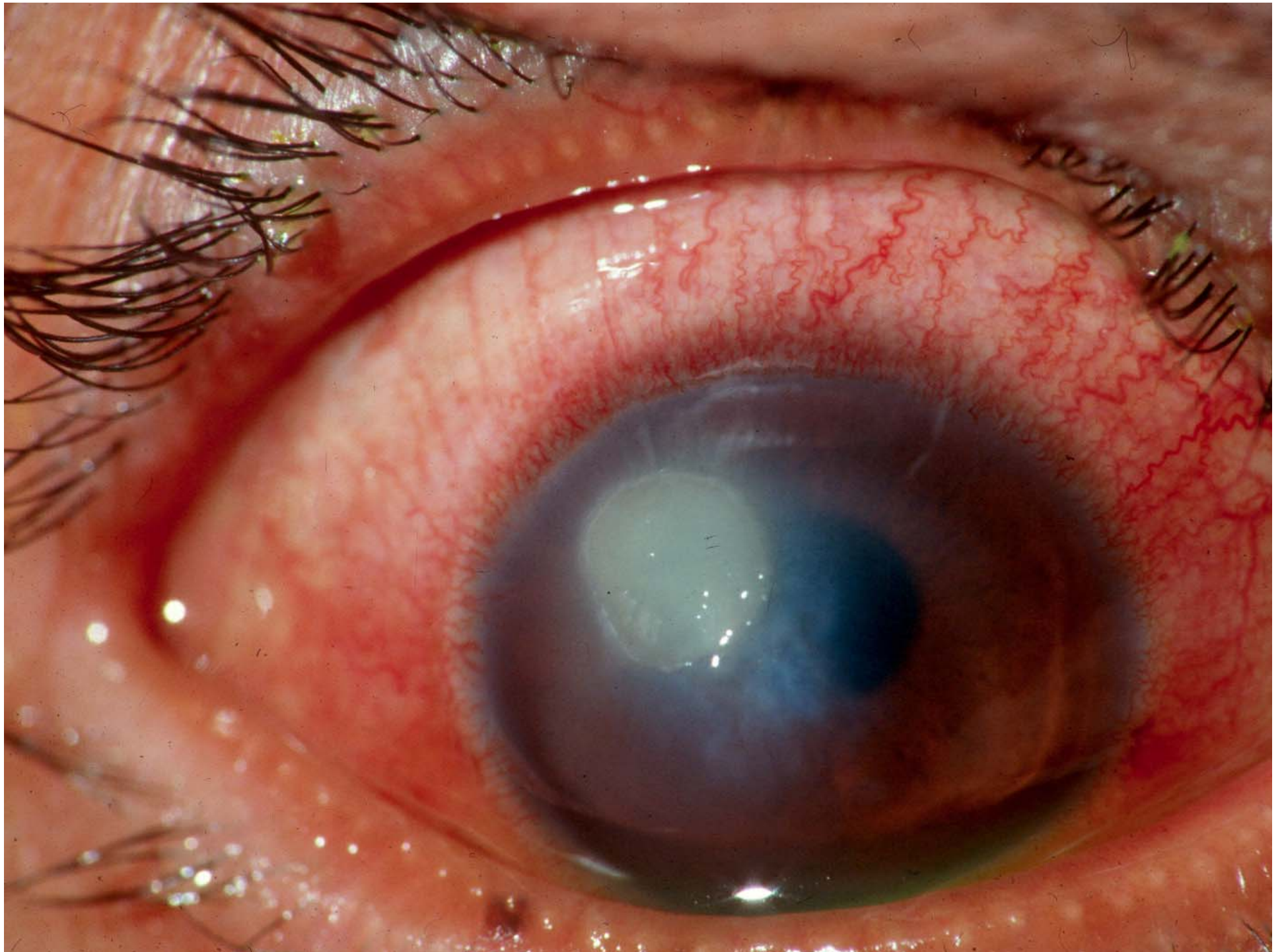
Keratoconus

Anterior polar cataracts

Mucous discharge

Atopic blepharitis





Vernal Keratoconjunctivitis (VKC)

Causes:

Genetic predisposition, atopy
Seasonal/perennial allergens (IgE)
Nonspecific hypersensitivity

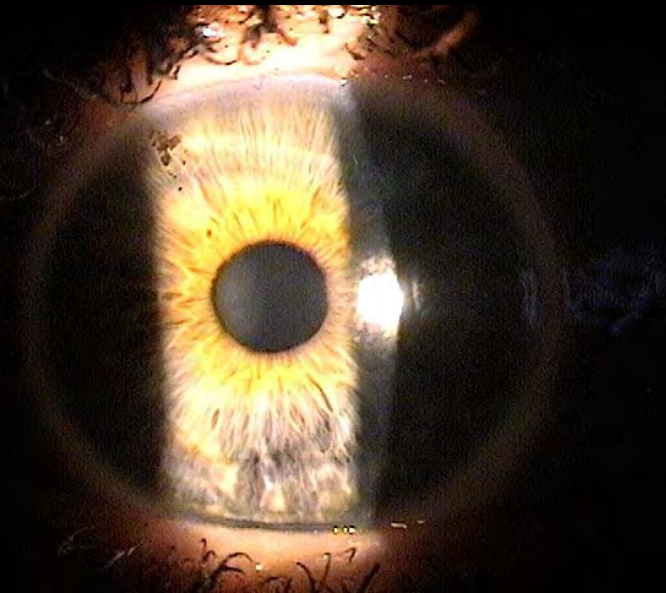
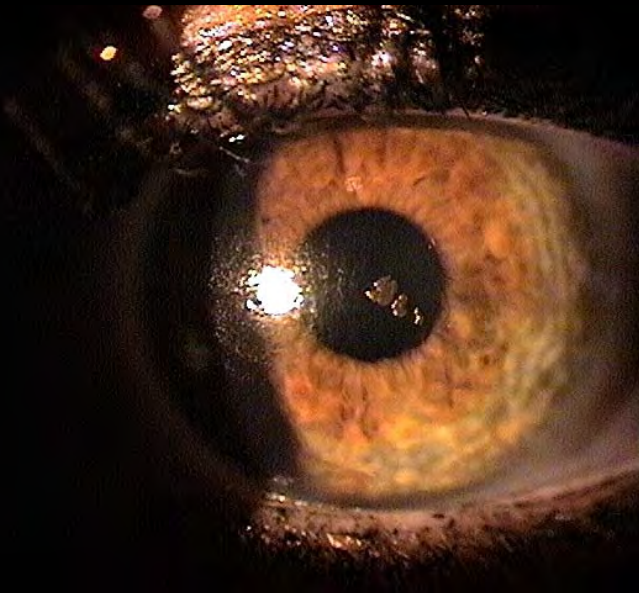
Clinical Findings:

Most predominant in males from 3 to 20 years old
Increased levels of superficial mast cells, eosinophils, and lymphocytes
Decreased levels of histaminase

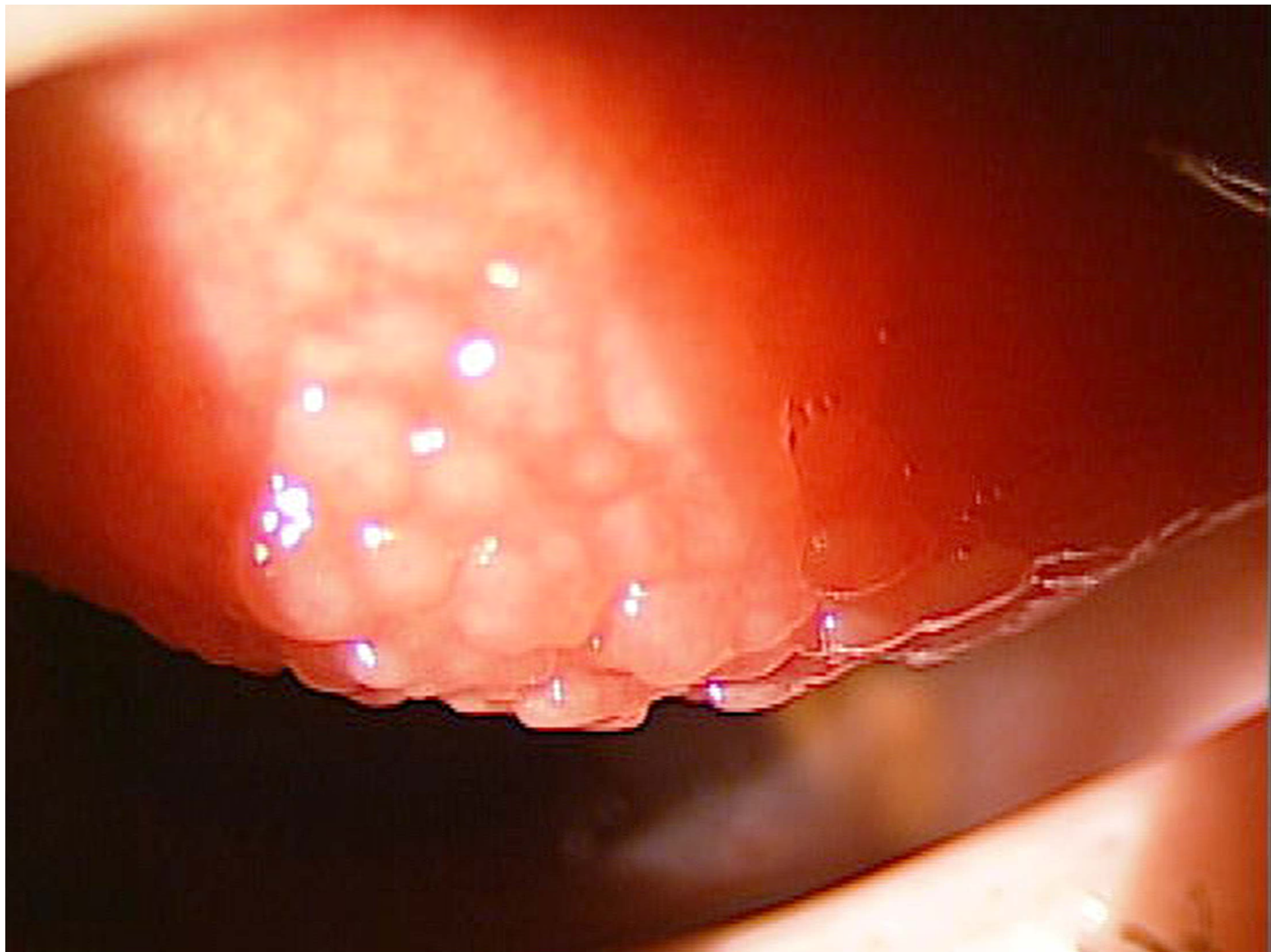
Signs/Symptoms:

Ptosis
Ropy mucous discharge
Photophobia
Large, nonuniform cobblestone papillae
Trantas dots
Limbal nodules
Neovascularization
Shield ulcers
Itching

Contact Lenses







Giant Papillary Conjunctivitis (GPC)

Causes:

**Repeated mechanical irritation
caused by:**

- Contact lens edge**
- Exposed sutures**
- Extruded scleral buckle**
- Ocular foreign bodies**

**Aggravated by concomitant
allergy**

**Can also aggravate ocular
allergy**

Clinical Findings:

**Increased chronic inflammatory
cells**

Signs/Symptoms:

- Decreased CL tolerance**
- Blurred vision**
- Foreign body sensation**
- Small, uniform papillae
on upper tarsal plate**
- Thick mucous build-up**

Peroxide Solutions



Store Brand Peroxide



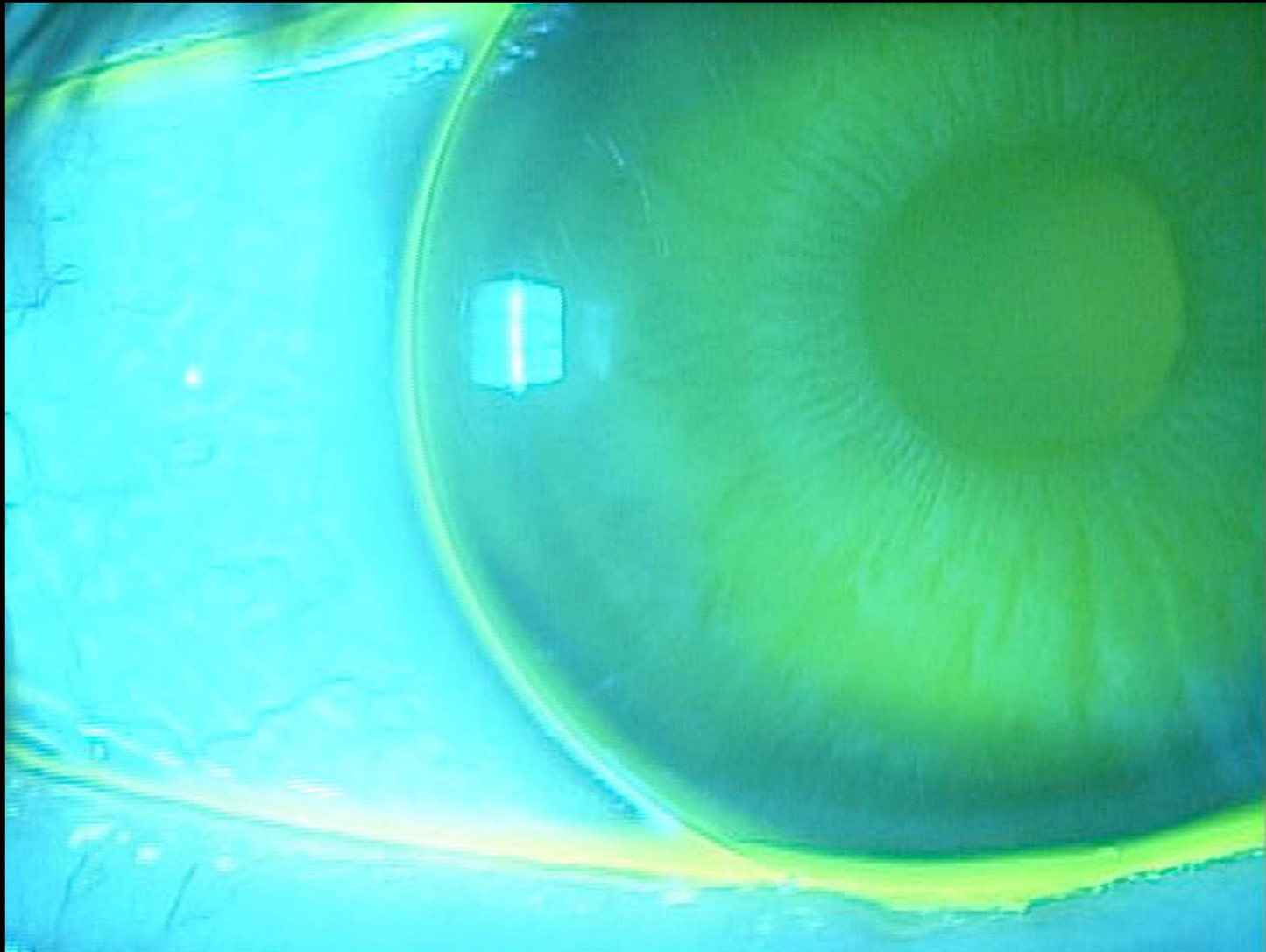
Peroxide Vials



Peroxide Vials



RGP's



Treatment Options

- Topical Medications
 - Antihistamine/ Mast Cell Stabilizer Combinations
 - Blocks Histamine receptors on blood vessels, nerve endings, etc
 - Inhibits histamine degranulation from sensitized mast cells so that when these cells are challenged with antigen, they do not degranulate
 - Patanol, Pataday, Elestat, Zaditor, Lastacraft, Bepreve

0.1%



0.2%



0.7%



Zerviate

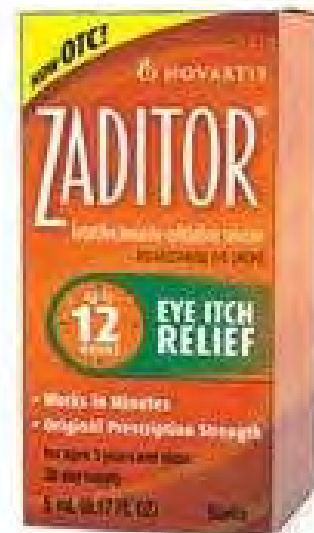
- Cetirizine ophthalmic solution 0.24%
- Available as oral agent (Zyrtec)
- Will be distributed through Eyevance
- First topical ophthalmic formulation of cetirizine
- Approved as bid dosing regimen



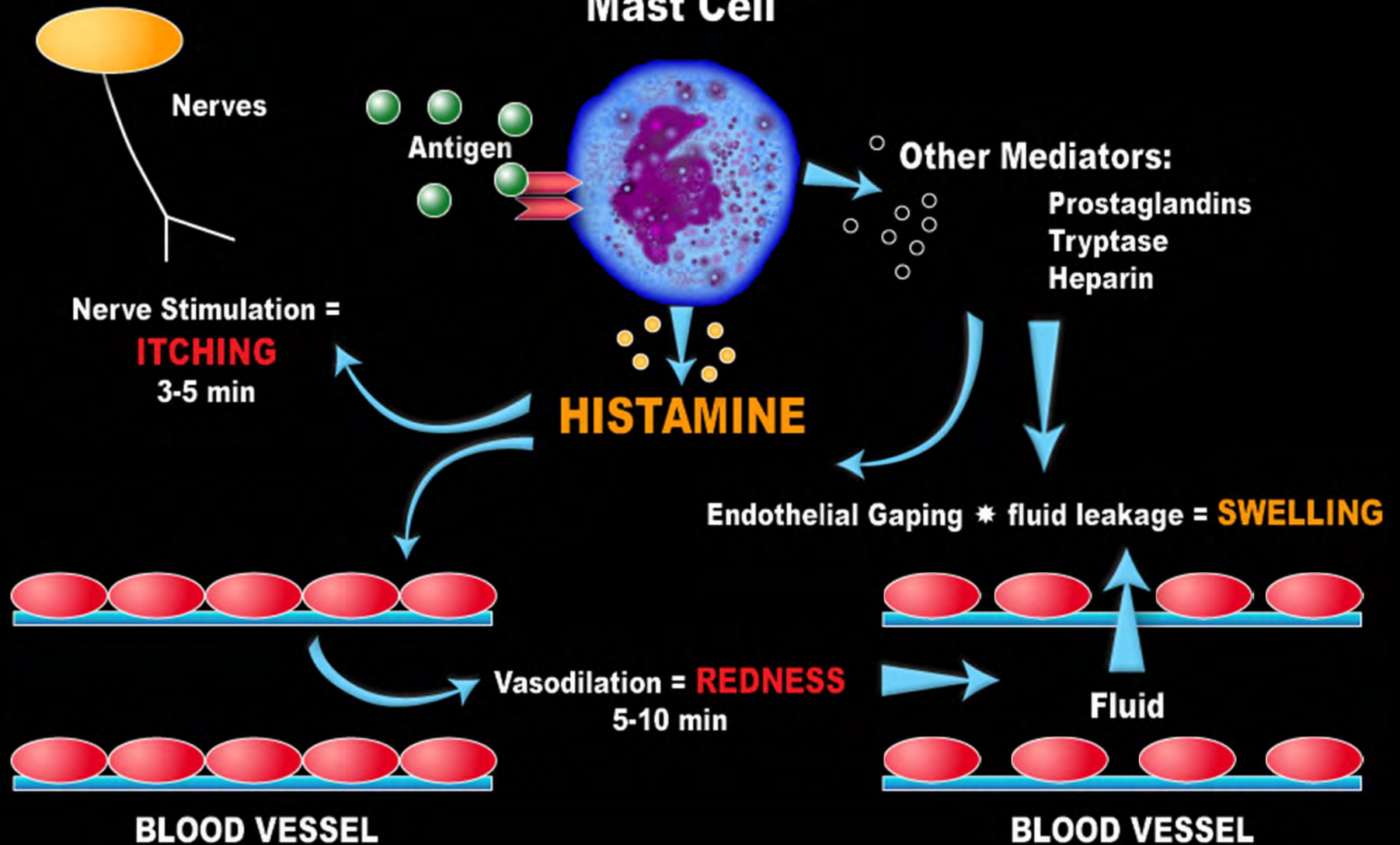
Olopatadine



Ketotifen



Degranulated Mast Cell

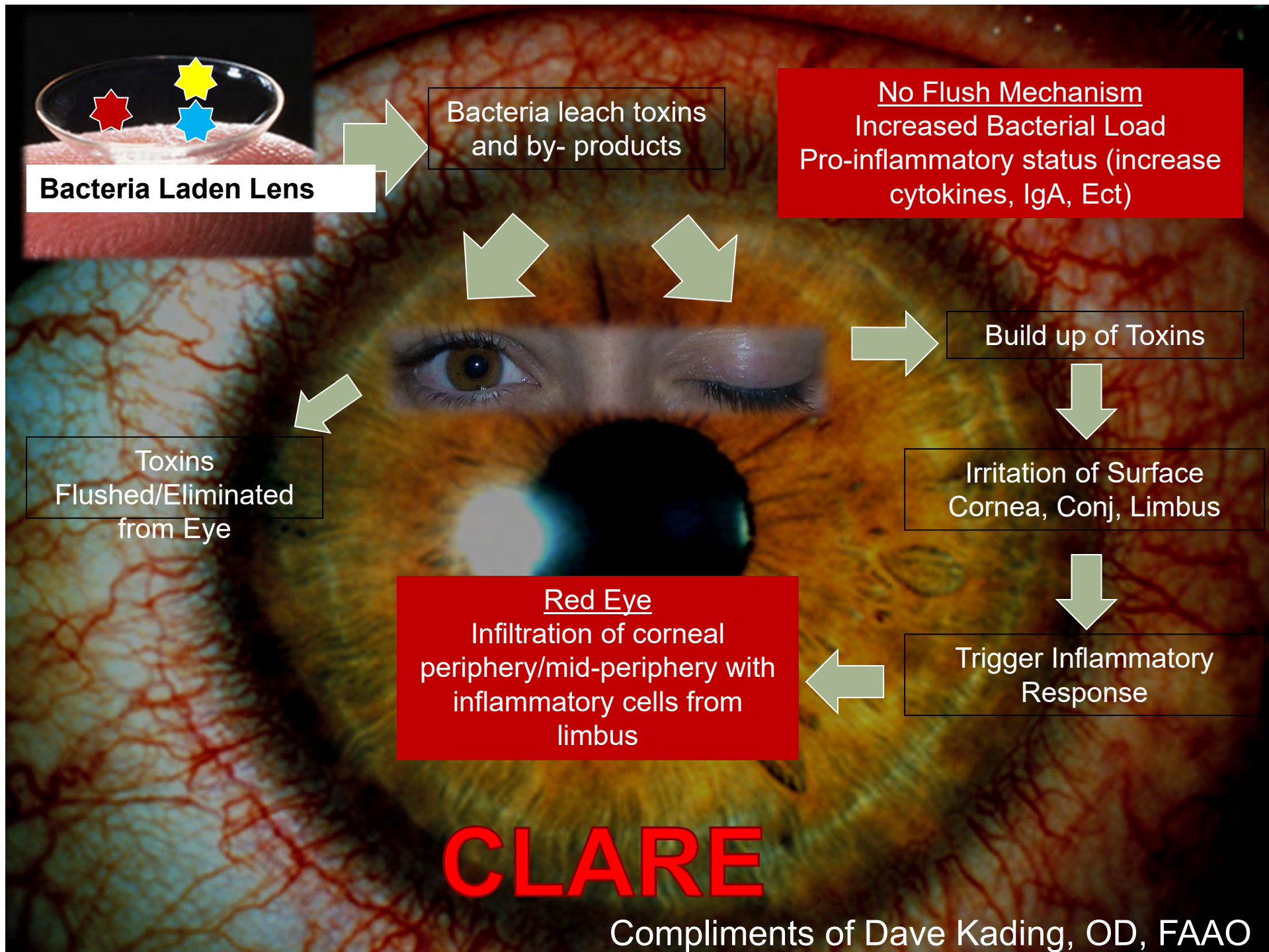


Treatment Options



Aldehyde Traps

- www.aldeyra.com
- Aldehyde is a product of metabolism
- Normally rapidly broken down
- With inflammation, is produced in quantities that are difficult to breakdown efficiently
- NS2 – an aldehyde trap molecule currently being investigated



sig: 1 gtt qid in the affected eye



Antibiotic steroid combinations



Infiltrates – Infectious vs. Inflammatory

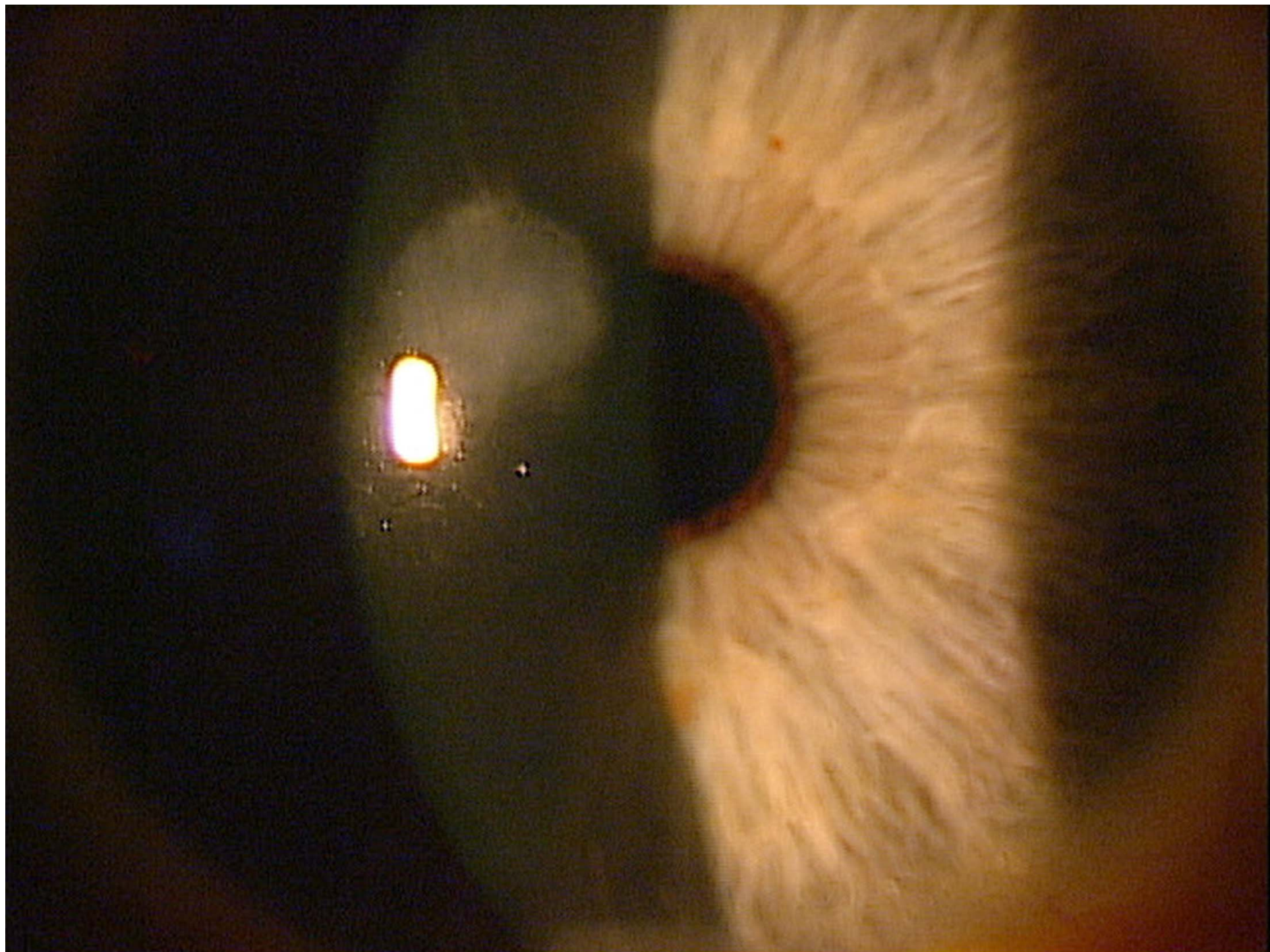
- Microbial Keratitis
 - Moderately severe symptoms, (+) corneal staining, (+) A/C reaction, (+) stromal edema, single infiltrate, purulent discharge
- Sterile Corneal infiltrates
 - Minimal to moderate symptoms, minimal corneal staining, minimal to no A/C reaction, little edema if present, multiple infiltrates, (-) purulent discharge

Multicenter Case-
Controlled Study of the
Role of Lens Materials and
Care Products on the
Development of Corneal
Infiltrates

Results

- The multivariate analysis found the following factors to be significant for the development of CIE's in contact lens wearers
- Reusable contact lenses
- Extended wear
- Younger age
- Silicone hydrogel lenses

Chalmers R, Keay L, McNally J, Kern J. Multicenter Case-Control Study of the Role of Lens Materials and Care Products on the Development of Corneal Infiltrates. *Optometry and Vision Science* 2012; 89(3): 316-325.



Corticosteroids for Bacterial Keratitis: The Steroids for Corneal Ulcers Trial (SCUT)

Corticosteroids for Bacterial Keratitis

- 500 patients enrolled with a culture positive bacterial ulcer
- All were treated with topical moxifloxacin 1 gt q1hr while awake for 48hrs then 1 gt q2hrs while awake until re-epithelialization occurs followed by 1 gt qid until 3 weeks after enrollment

Corticosteroids for Bacterial Keratitis

- Patients were randomized to either receive topical prednisolone sodium phosphate 1% or placebo after 48 hours of effective antibiotic treatment
- Steroid and placebo were dosed:
 - QID for the first week after treatment started
 - BID for the second week after treatment started
 - QD for the third week after treatment started

Corticosteroids for Bacterial Keratitis

- Patients were evaluated every 3 days until re-epithelialization, then 3 weeks and 3 months after enrollment
- No differences in BCVA, infiltrate scar size and re-epithelialization rates between test and control arm

Corticosteroids for Bacterial Keratitis

- Subgroup analysis:
- Those with significantly reduced entering visual acuity (CF or worse)
 - 0.17 better logMAR improvement with steroids
- Ulcers completely covering the 4 mm pupil
 - 0.2 better logMAR improvement with steroids

Emergency Visit

- 35 year old male called into the office earlier that morning
- Has had a painful red left eye for the past 10 days
- Saw his primary care physician about 1 week ago
- They prescribed a drop that he has been using qid in the eye – feels like it is getting worse
- Meds – none
- Allergies – NKA
- Review of Systems - negative

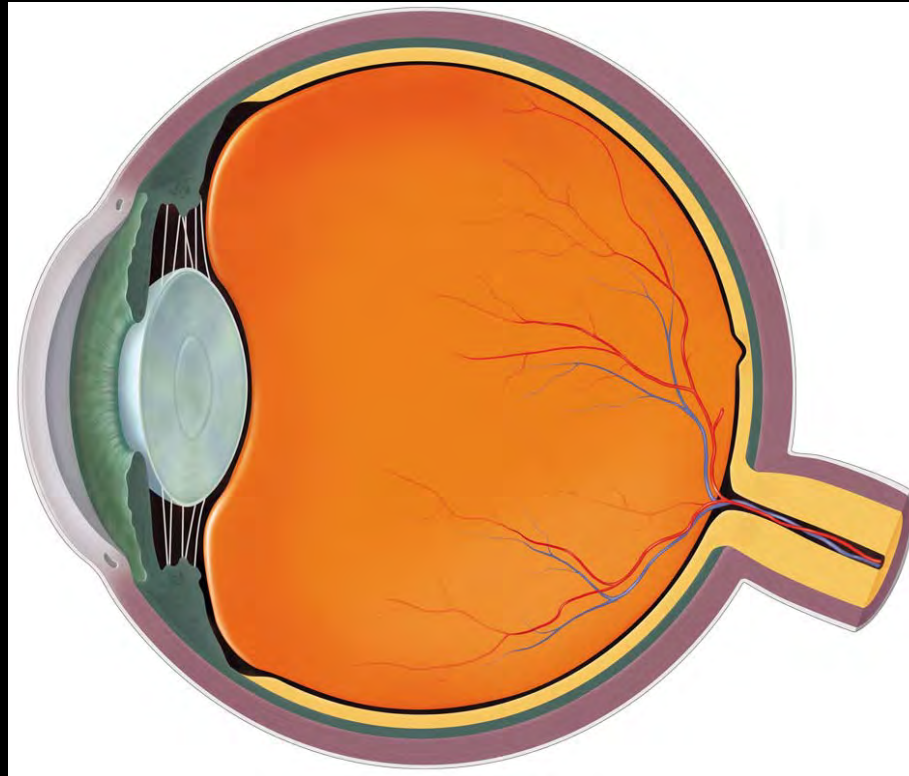
Examination

- Mild eyelid hyperemia
- Preauricular lymph nodes are negative
- +3 injection OS
- No corneal staining present; prominent stromal scar (longstanding)
- Pupils – RRL; OD>OS
- IOP – 16mmHg @ 11:00am

Uveitis

- 8 per 100,000
- 90% are acute anterior uveitis
- Majority of primary cases are idiopathic

Uvea

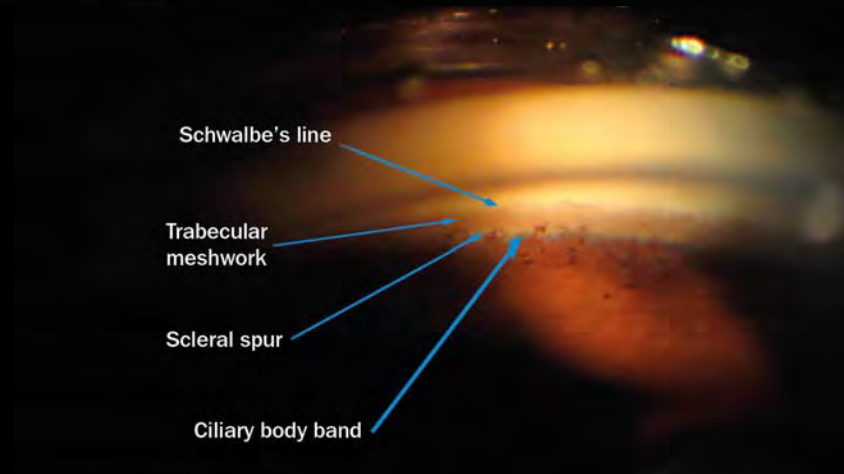
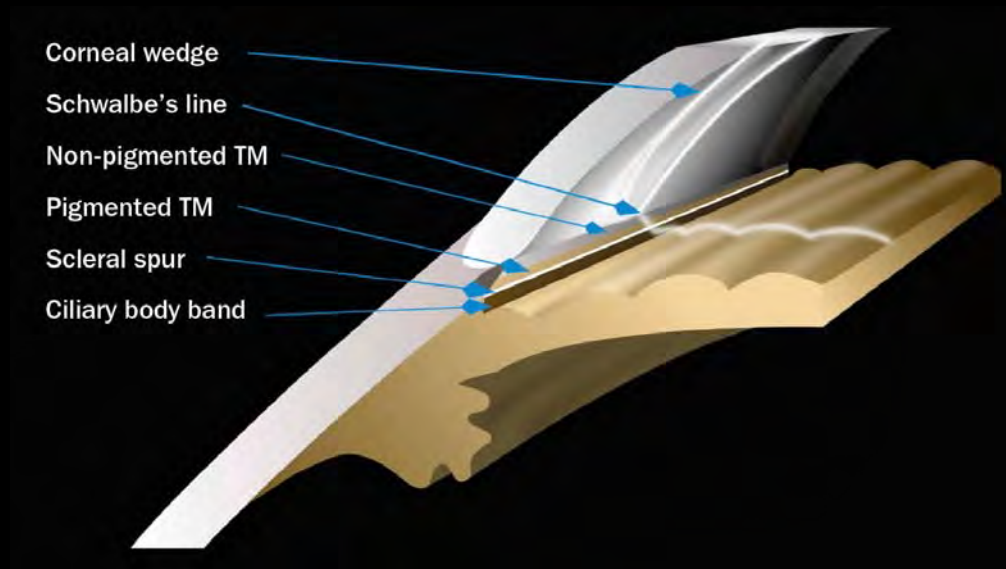


What is inflammation

- Cyclooxygenase
 - COX-1 and COX-2
 - COX-1 – normal physiological response (stomach)
 - COX-2 – facultatively expressed - inflammation
- COX produces prostaglandins and thromboxanes from arachidonic acid
- Arachidonic acid is produced via phospholipase A

What if IOP is increased?

- Is it caused by angle closure?
- Is it caused by trabeculitis?
- Is there another entity that is causing elevated IOP?
- www.gonioscopy.org



Indian Journal of Ophthalmology

Indian J Ophthalmol. 58(1): 11-19

Current approach in diagnosis and management of anterior uveitis

Rupesh V Agrawal, Somasheila Murthy, Virender Sangwan, Jyotirmay Biswas¹

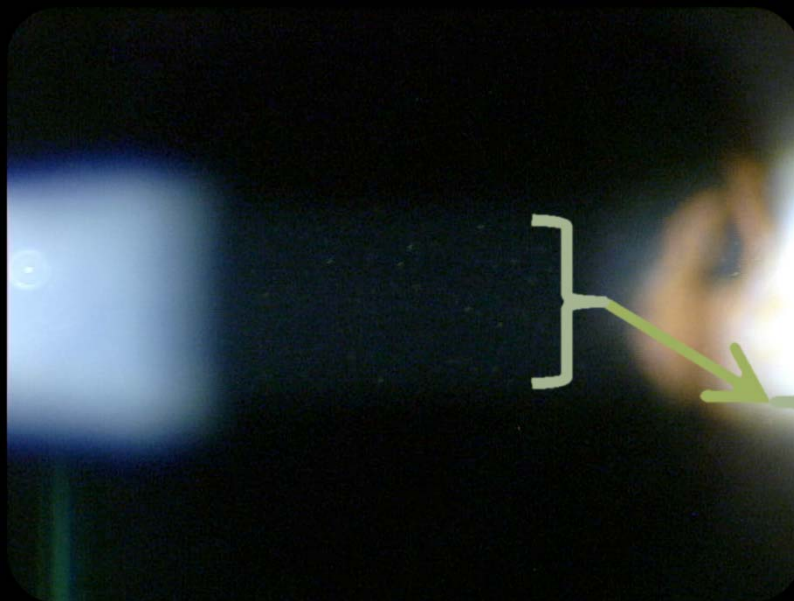
L. V. Prasad Eye Institute, Kallam Anji Reddy Campus, Hyderabad, India

1. Medical Research Foundation, Sankara Netralaya, Chennai, India

SUN Working Grouping Grading of cells and flare

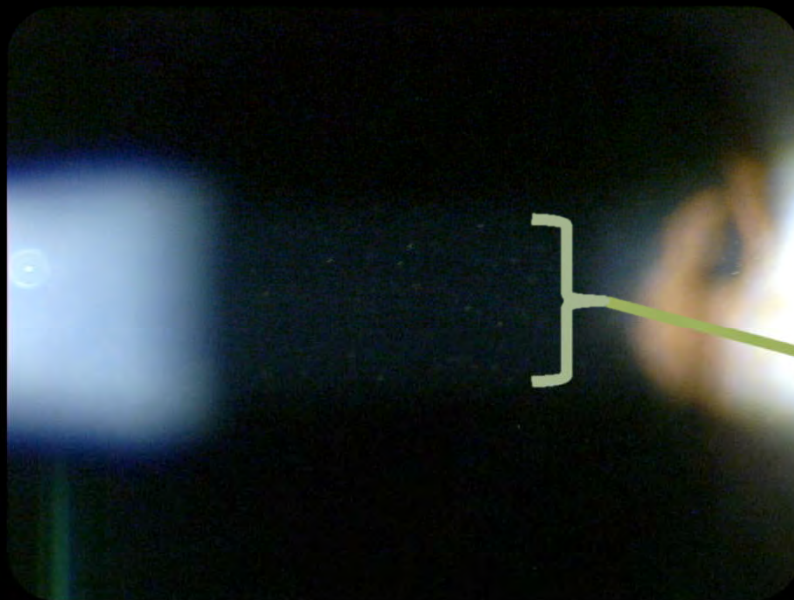
AC Flare	Grade	Cells/ field
0-None	0-	<1
	0.5	1-5
1+ Faint	1+	6-15
2+ Moderate (Iris and lens details clear)	2+	16-25
3+ Marked (Iris and lens details clear)	3+	26 -50
4+ Intense (Fixed and plastic aque- ous)	4+	50+

Slit Lamp Evaluation



AC Flare	Grade
0-None	0-
	0.5
1+ Faint	1+
2+ Moderate (Iris and lens details clear)	2+
3+ Marked (Iris and lens details clear)	3+
4+ Intense (Fixed and plastic aqueous)	4+

Slit Lamp Evaluation



Grade	Cells/ field
0-	<1
0.5	1-5
1+	6-15
2+	16-25
3+	26-50
4+	50+

Anterior Uveitis

- Keratic Precipitates
 - Granulomatous vs. non-granulomatous
- Constricted Pupil
- Iris Nodules
 - Koeppe's nodules
 - Pupillary margin
 - Busaca's nodules
 - Anterior iris stroma

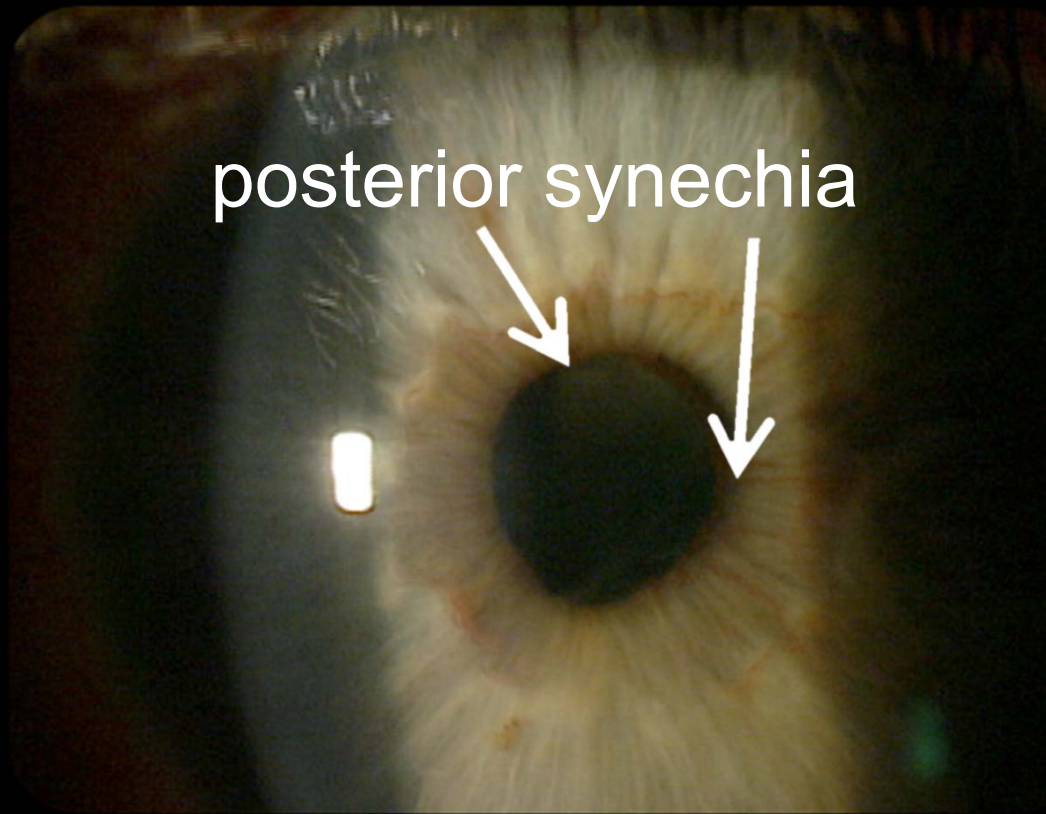
Posterior Synechiae

- Attachment of the iris to the lens
- Usually secondary to inflammatory components
- Can create an angle closure through pressure that builds up behind the iris causing it to bow anteriorly causing a physical obstruction to the angle
- Visible white inflammatory debris seen on the lens at the edge of the iris

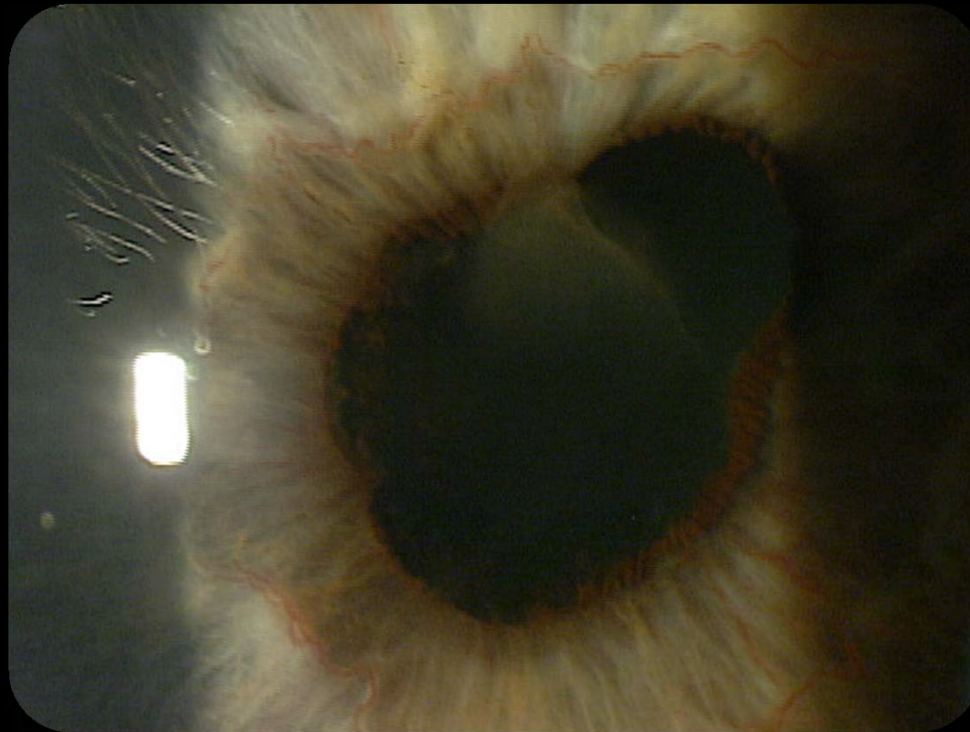
Posterior Synechiae

- Measure intraocular pressure
- View angles
- Consider gonioscopy if suspicious of blocked angle secondary to an iris that is bowed forward

Slit Lamp Evaluation



15 minutes post cycloplegic



Intraocular Pressure

- Can be decreased
 - Inflammation of the ciliary body
 - Will decrease aqueous production and decrease IOP
- Can be elevated
 - Trabeculitis
 - Will increase resistance to outflow and increase IOP
 - Can also be secondary to angle closure

What's the next step?



Topical Corticosteroids



Thank You

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