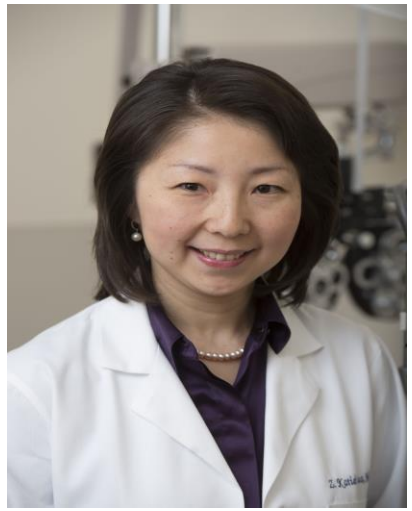
Graft-versus-Host Disease: What to Do When It Affects Your Eyes

Celebrating a Second Chance at Life Survivorship Symposium

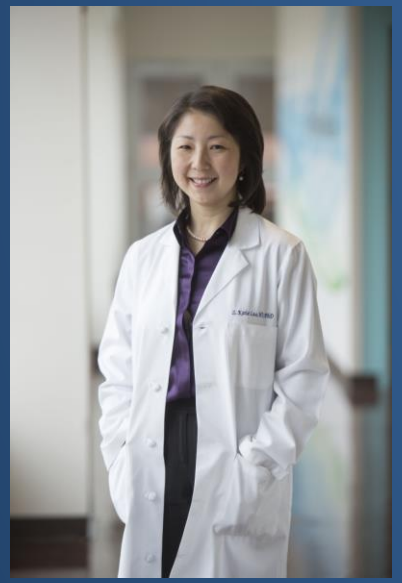
May 3-9, 2025



Zhonghui Katie Luo, MD, PhD
Massachusetts Eye and Ear

Ocular Graft versus Host Disease

What to do when it affects your eyes



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May 4th, 2025

Summary

- What is ocular GvHD
- How does it happen
- Early signs
- Management

Warning!
Some patients find some of the images scary

Graft vs. Host Disease

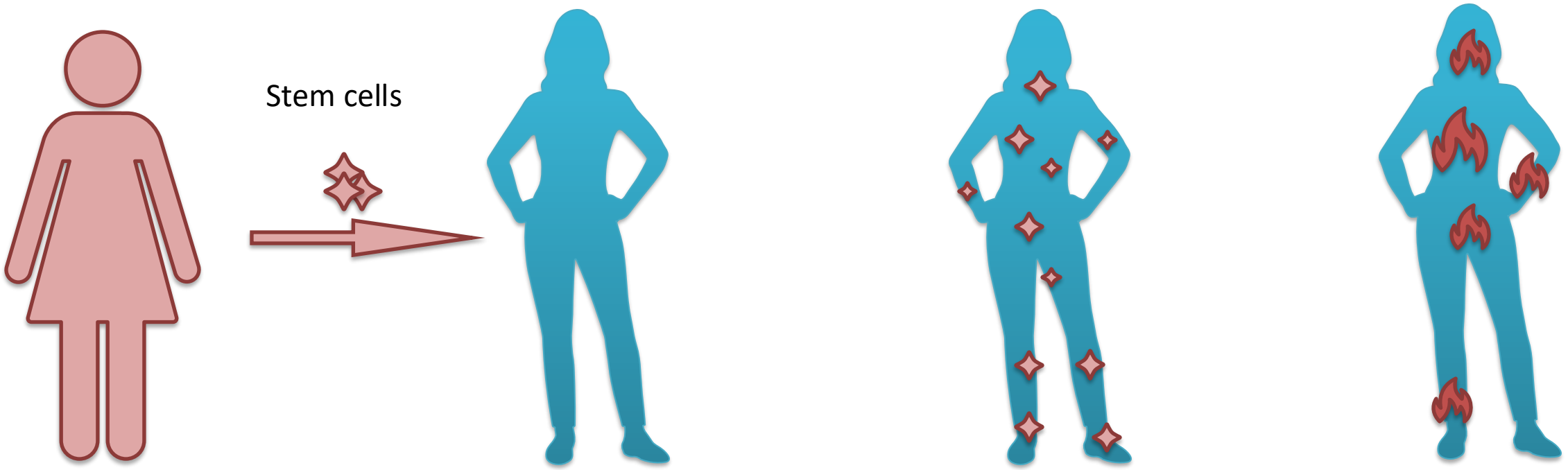
Donor

Stem cells

Host/recipient

New immune system forms

Attack host organs



Ocular GvHD

- Ocular GvHD affects 40-60% of patients after allo-HSCT
- Often underdiagnosed
- It can occur along with chronic GvHD of other organs or independently

Acute Ocular GvHD

Most often occurs within first 3 months after HSCT, but can be much later

- skin rash
- elevated liver enzymes
- digestive system dysfunction

The eyes can be significantly affected

Chronic Ocular GvHD

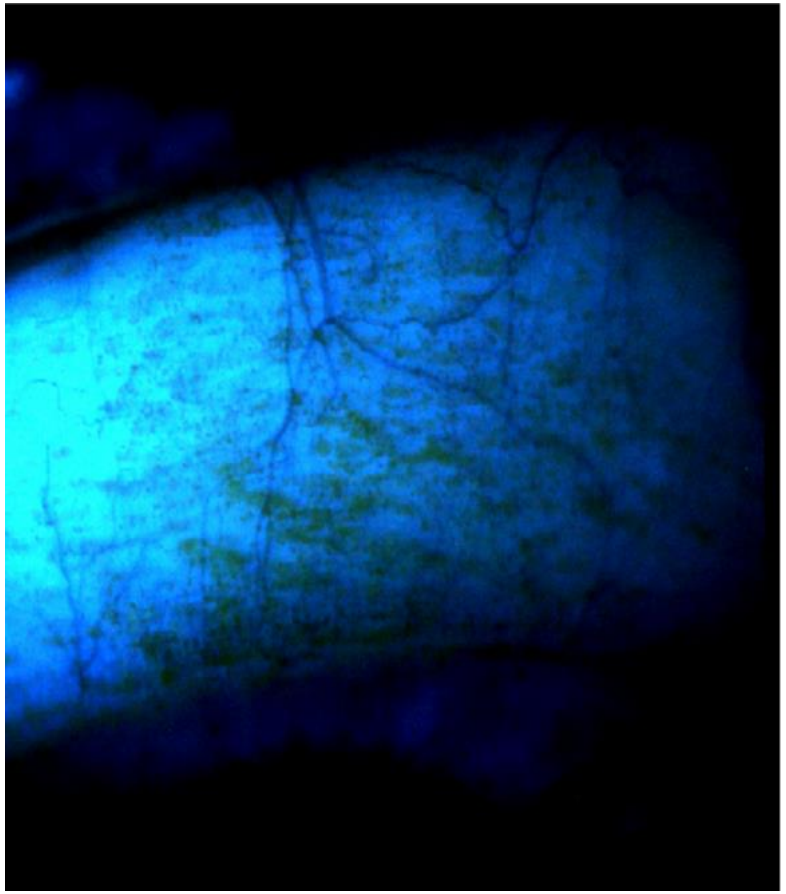
- The more common presentation, often referred to simply as oGVHD

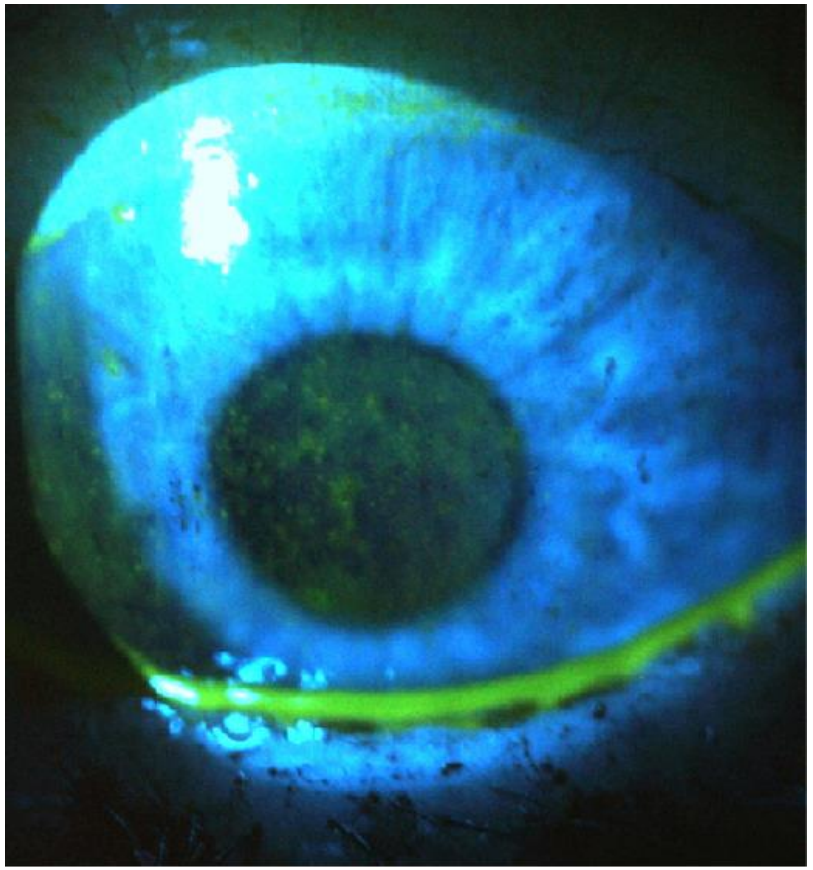
- Most often onset three months to two years after HSCT, but can be a few weeks to more than a decade

- Can be isolated, first sign or later ~~sign among other~~ GvHD

- *Squinting*
- *Sunglasses indoor*
- *Hands over brows*
- *Poor functional vision*

Very Dry Eyes (the best recognized sign but a LATE sign)





Very Early Events (easily missed!)

A typical story:

Eyes were fine through the transplant

↓

Suddenly became watery/wet

↓

Morning crusting so much the lashes stuck together

↓

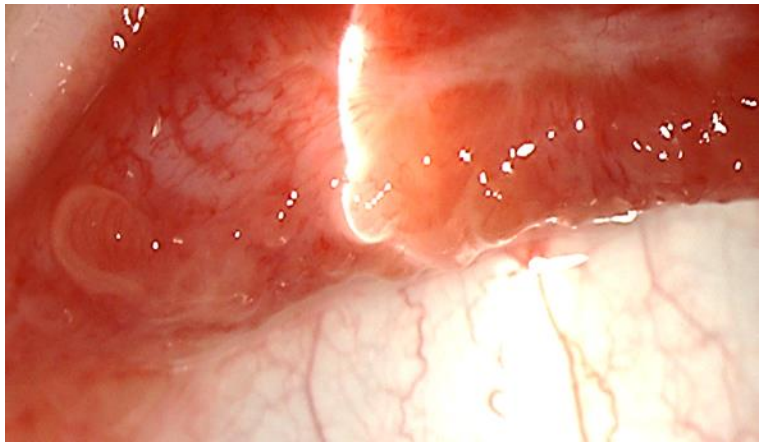
With or without gritty sensation

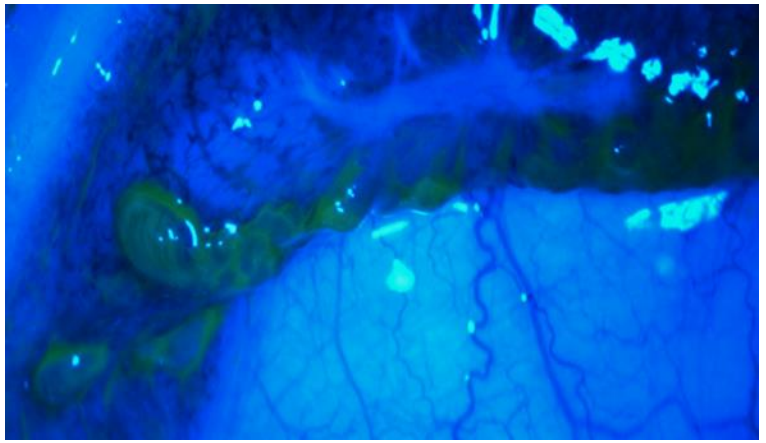
↓

Typically, not very bothersome

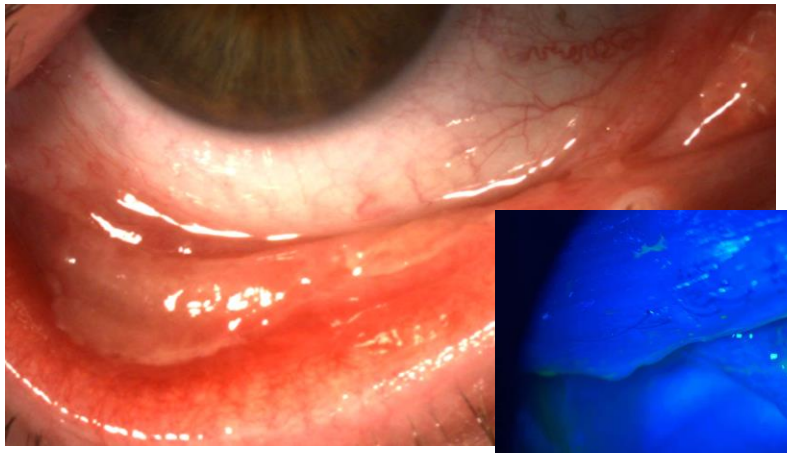
↓

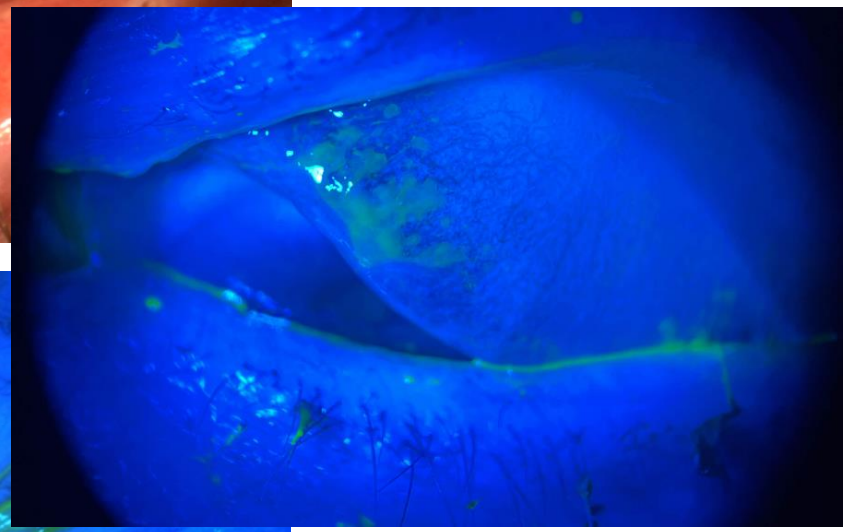
Rarely reported to their BMT doctor

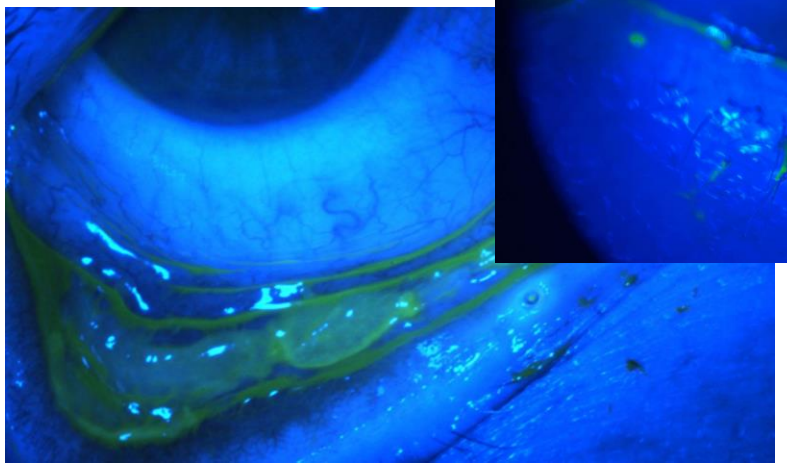




It Looks Like a Milder Version of Acute oGVHD



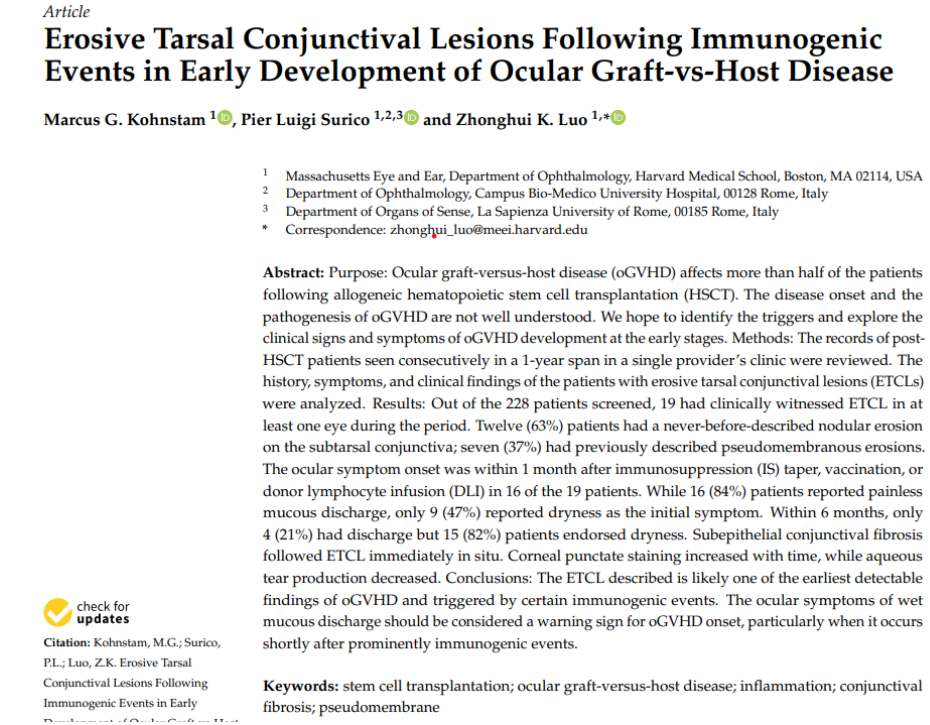




Very early detection

New fibrosis 4 weeks after treatment

Ocular symptoms started within 1 month after highly immunogenic events



Article

Erosive Tarsal Conjunctival Lesions Following Immunogenic Events in Early Development of Ocular Graft-vs-Host Disease

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Abstract: Purpose: Ocular graft-versus-host disease (oGVHD) affects more than half of the patients following allogeneic hematopoietic stem cell transplantation (HSCT). The disease onset and the pathogenesis of oGVHD are not well understood. We hope to identify the triggers and explore the clinical signs and symptoms of oGVHD development at the early stages. Methods: The records of post-HSCT patients seen consecutively in a 1-year span in a single provider's clinic were reviewed. The history, symptoms, and clinical findings of the patients with erosive tarsal conjunctival lesions (ETCLs) were analyzed. Results: Out of the 228 patients screened, 19 had clinically witnessed ETCL in at least one eye during the period. Twelve (63%) patients had a never-before-described nodular erosion on the subtarsal conjunctiva; seven (37%) had previously described pseudomembranous erosions. The ocular symptom onset was within 1 month after immunosuppression (IS) taper, vaccination, or donor lymphocyte infusion (DLI) in 16 of the 19 patients. While 16 (84%) patients reported painless mucous discharge, only 9 (47%) reported dryness as the initial symptom. Within 6 months, only 4 (21%) had discharge but 15 (82%) patients endorsed dryness. Subepithelial conjunctival fibrosis followed ETCL immediately in situ. Corneal punctate staining increased with time, while aqueous tear production decreased. Conclusions: The ETCL described is likely one of the earliest detectable findings of oGVHD and triggered by certain immunogenic events. The ocular symptoms of wet mucous discharge should be considered a warning sign for oGVHD onset, particularly when it occurs shortly after prominently immunogenic events.

Keywords: stem cell transplantation; ocular graft-versus-host disease; inflammation; conjunctival fibrosis; pseudomembrane

check for updates

Citation: Kohnstam, M.G.; Surico, P.L.; Luo, Z.K. Erosive Tarsal Conjunctival Lesions Following Immunogenic Events in Early

Patient#	Symptom onset (months after HSCT)	IS taper (months before symptom onset)	Vaccination (months before symptom onset)	DLI (months before symptom onset)
1	5.6	0.5	-	-
2	12.6	4.3	-	0.6
3	5.6	0.6	0.9 (COVID)	-
4	Unclear	Unclear	-	-
5	21.4	4	0.8 (COVID)	-
6	10.5	0.6	0.7 (COVID)	-
7	9	1.2	-	-
8	6.3	0.3	-	-
9	10.5	1	-	-
10	9	0.9	-	-
11	9.6	-	0.8 (Bundle)	-
12	4.4	1.1	-	-
13	9.7	0.5	0.5 (Bundle)	-
14	8	0.2	-	-
15	9.6	4	1 (COVID)	-
16	8.8	1	2	-
17	9.1	2.9	0.1 (Bundle)	-
18	8	2.3	0.3 (COVID)	-
19	9.6	0.6	0.9 (Bundle)	-

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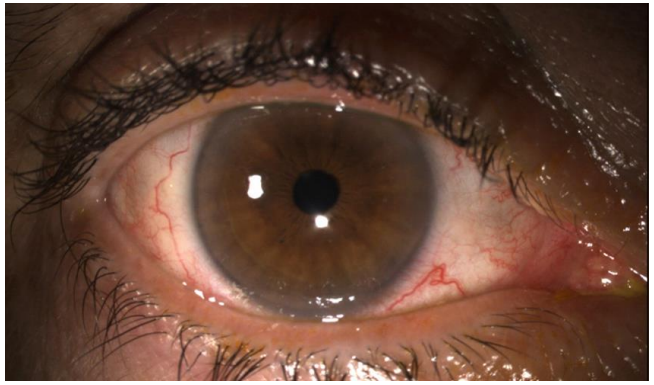
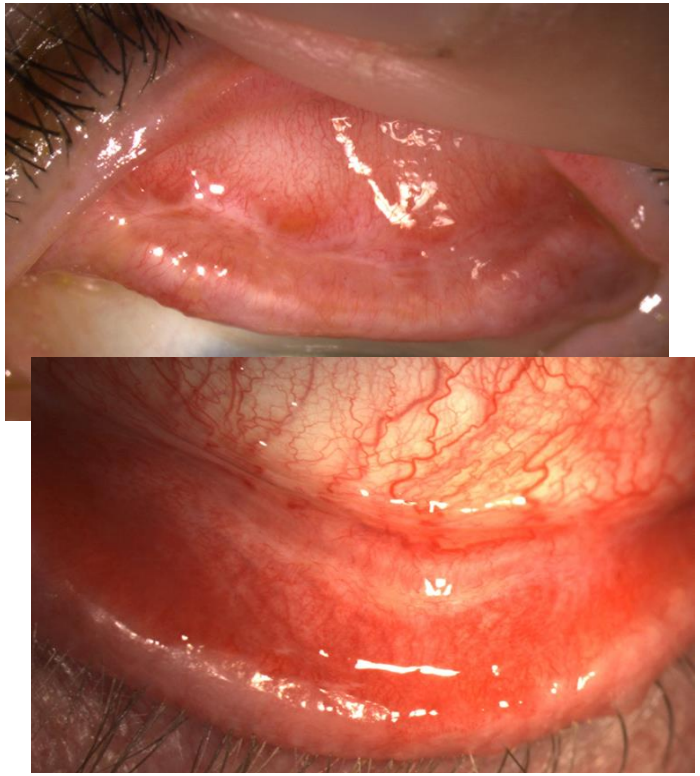
Sequence of Events Before Dry Eye Onset

In a quiet looking eye



Erosions can be hidden

Then turn into scars



Symptoms Change Over Time

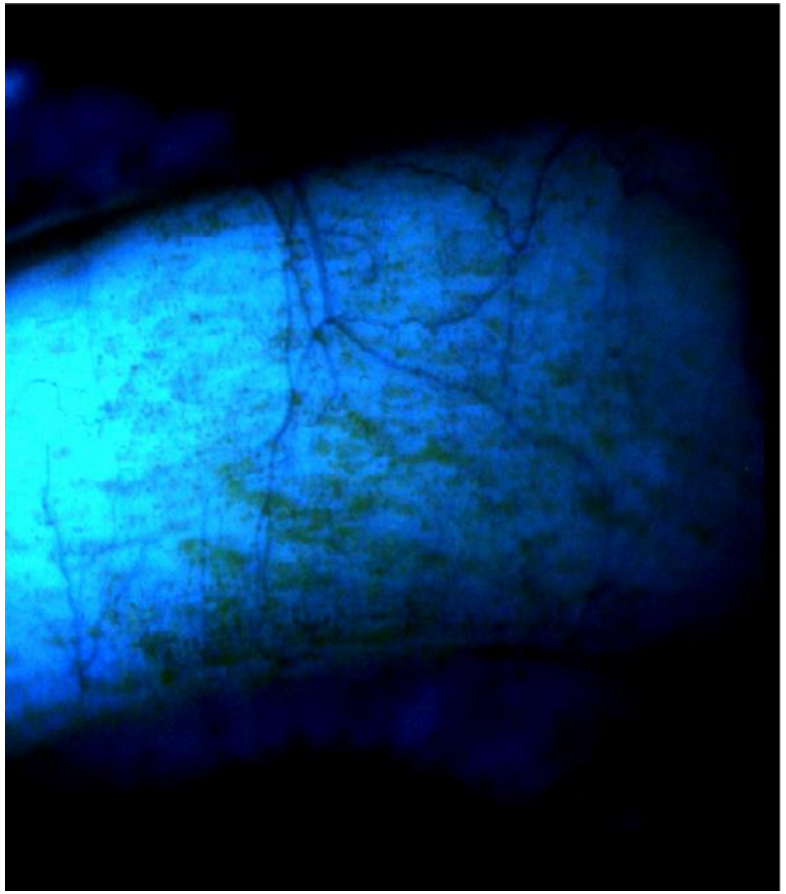
	At onset	At 6 months
Mucous discharge	16 (84%)	4 (31%)
Heavy morning crusting	15 (79%)	3 (23%)
Dryness	9 (47%)	10 (77%)
Irritation/Foreign body sensation	8 (42%)	9 (69%)

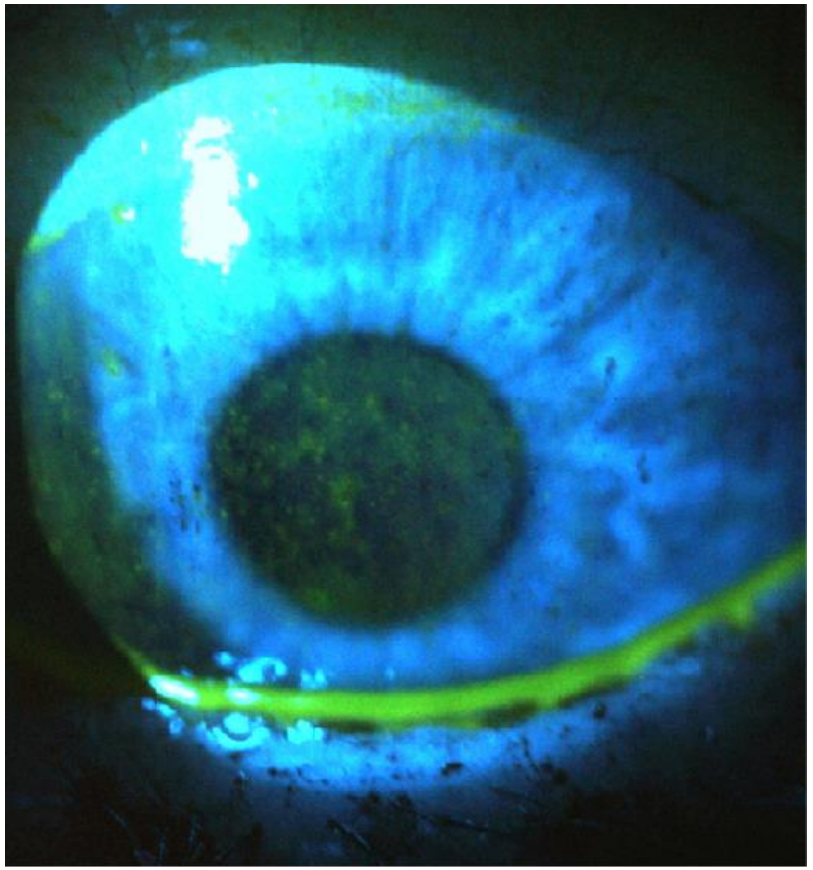
	During active erosion	After resolution (3-5 months later)
Tear Production(mm)	15 (0-35)	4 (0-13)

The Messages

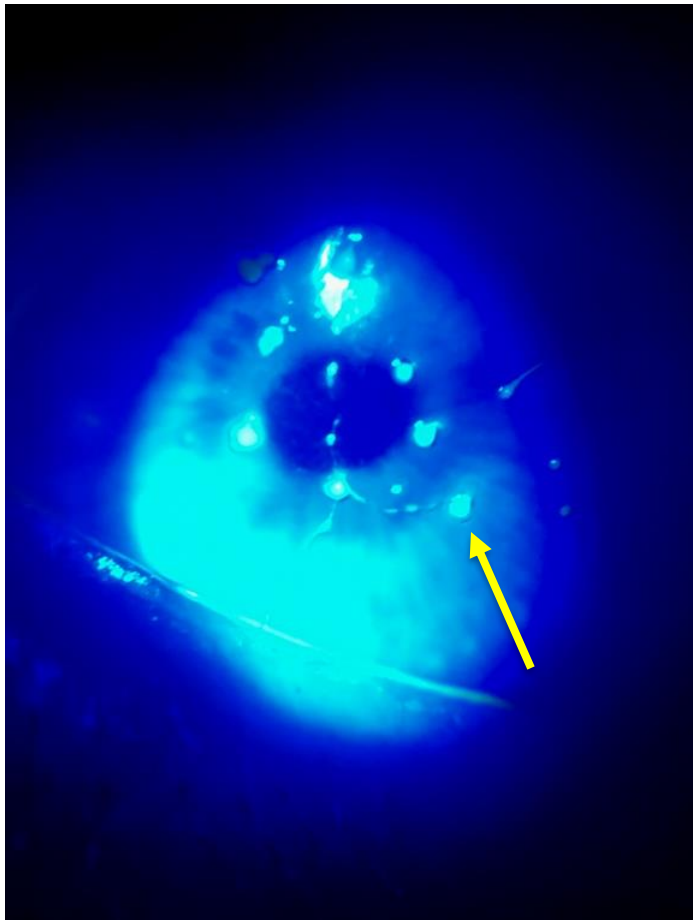
1. It is likely one of the earliest detectable signs of ocular GVHD – a new window of opportunity.
2. High clinical suspicion should be raised when post-HSCT patients reports mucous discharge or morning crusting, with or without dry eyes. Eyelid eversion should be performed.
3. Future prospective clinical studies should be designed to build in an eye exam within 1 month of highly immunogenic events (IS taper, Donor lymphocytes infusion, major vaccination etc.).

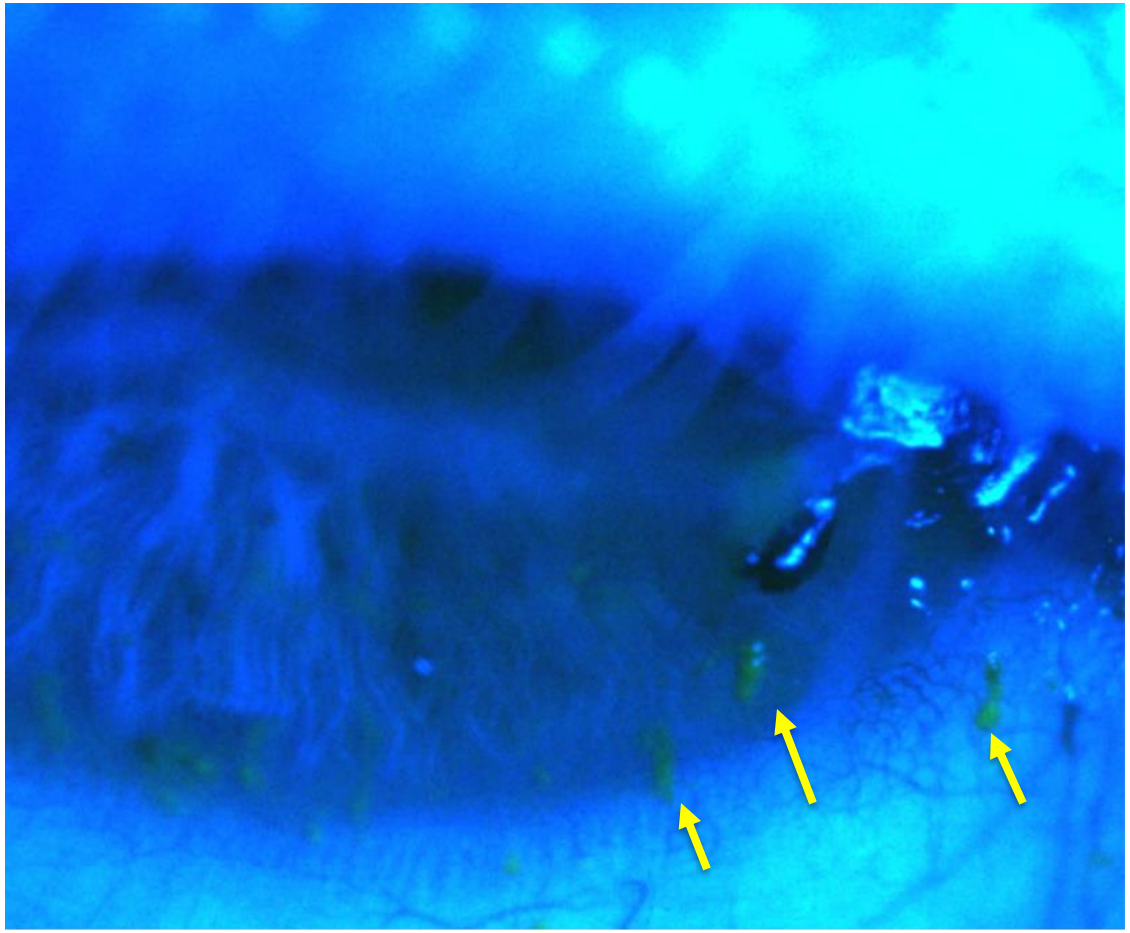
Very Dry Eyes (the best recognized sign but a LATE sign)





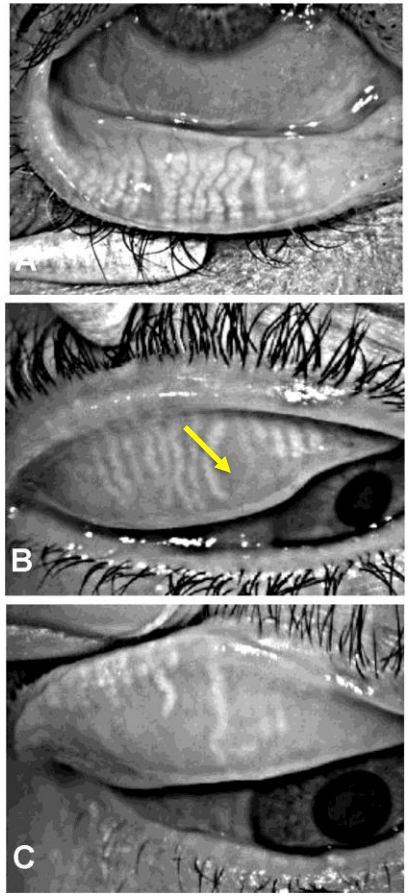
Filaments (they hurt a lot!)



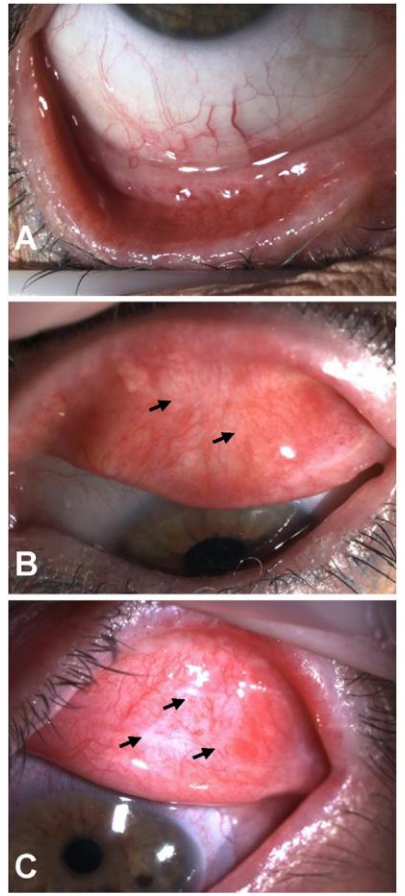


Important Glands on the Inside of the Lids are Damaged as Well

Destroyed meibomian glands



Conjunctival scars result of inflammation



Grade 1 (Mild)

Grade 2 (Moderate)

Grade 3 (Severe)

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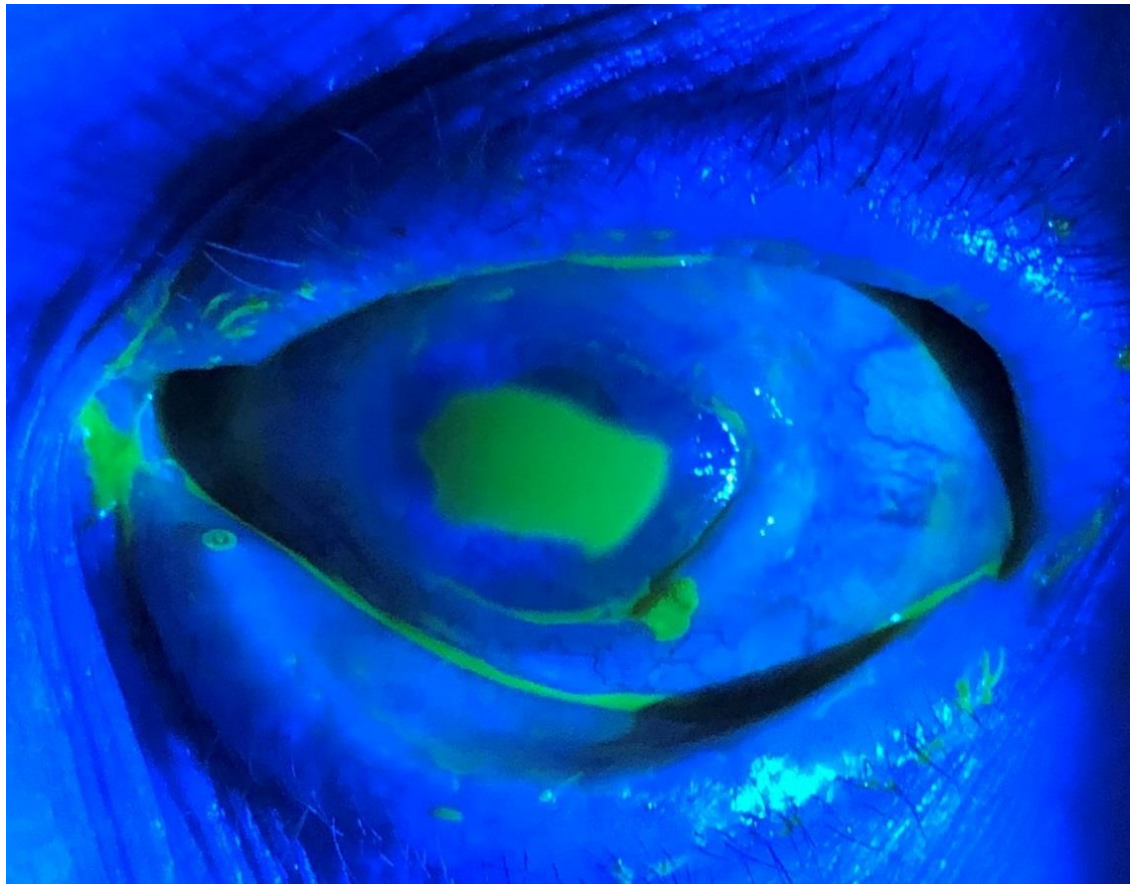
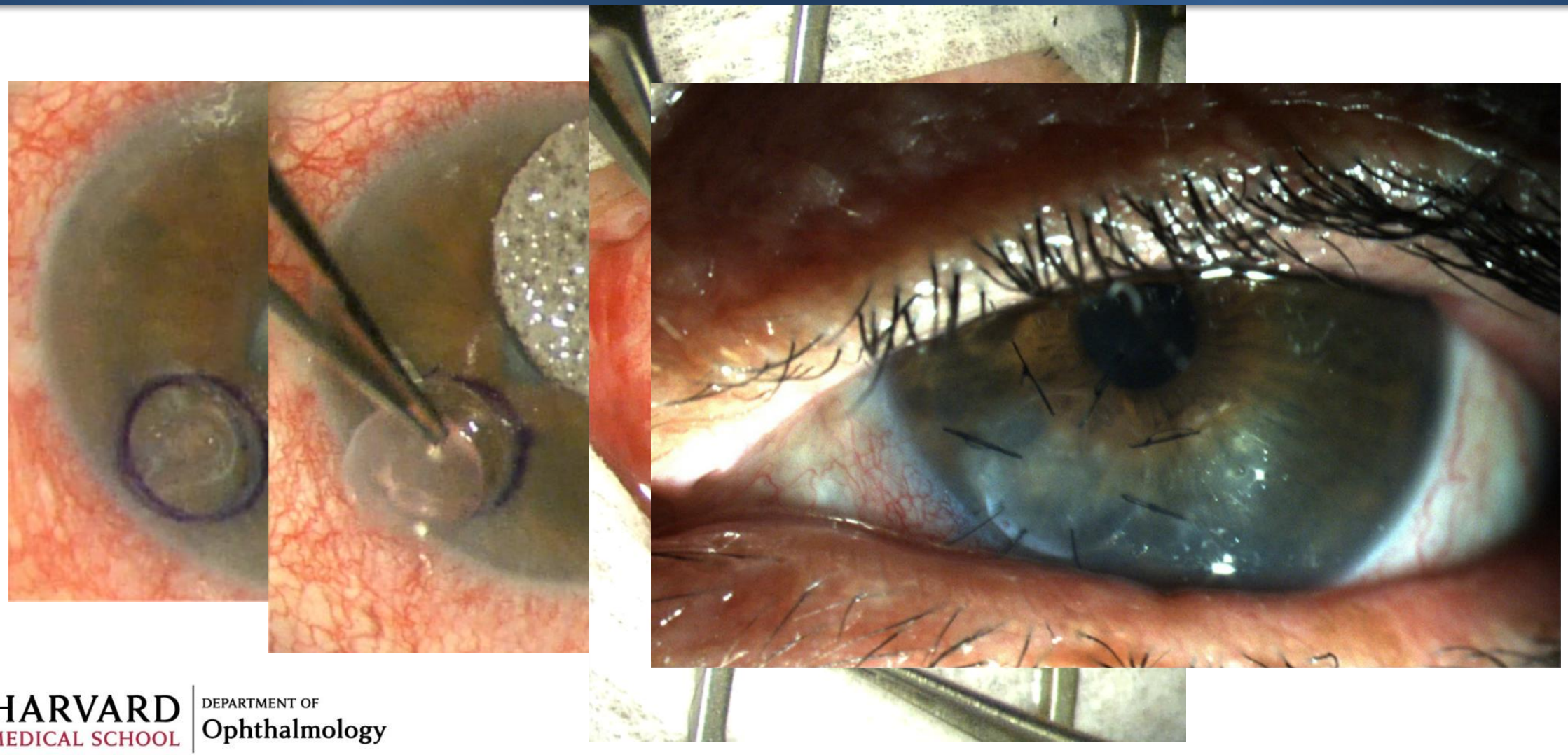
Kusne et al. 2017 Ocular Surface

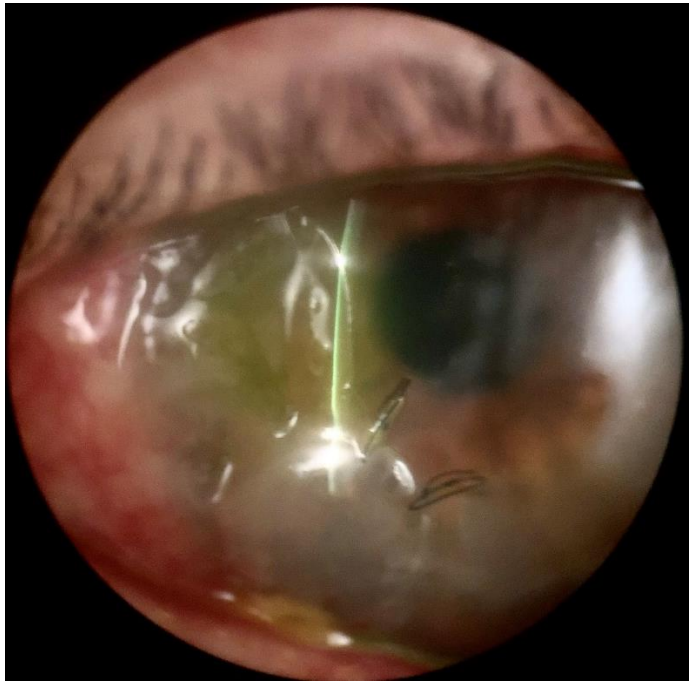
The surface breaks down when healing is severely compromised

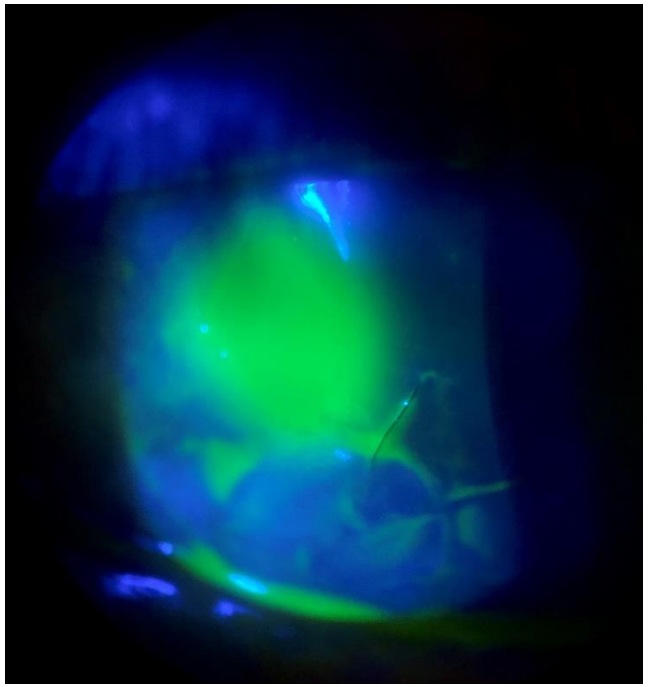


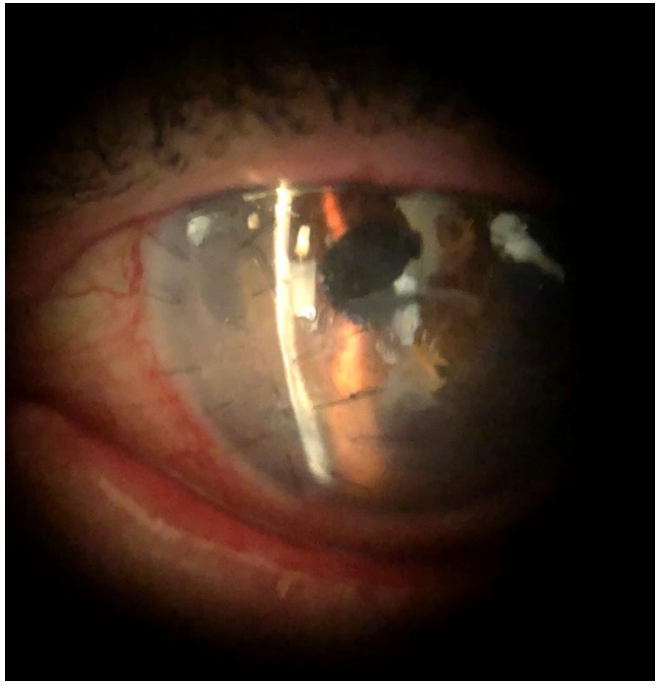
Cornea can perforate in just days



Keeps melting







What Can We Do about It?

First, understand the problems

Second, avoid preventable damage

Third, invest (your commitment) in management

Imbalance Between Damage and Repair

Inflammation

Tear glands damage

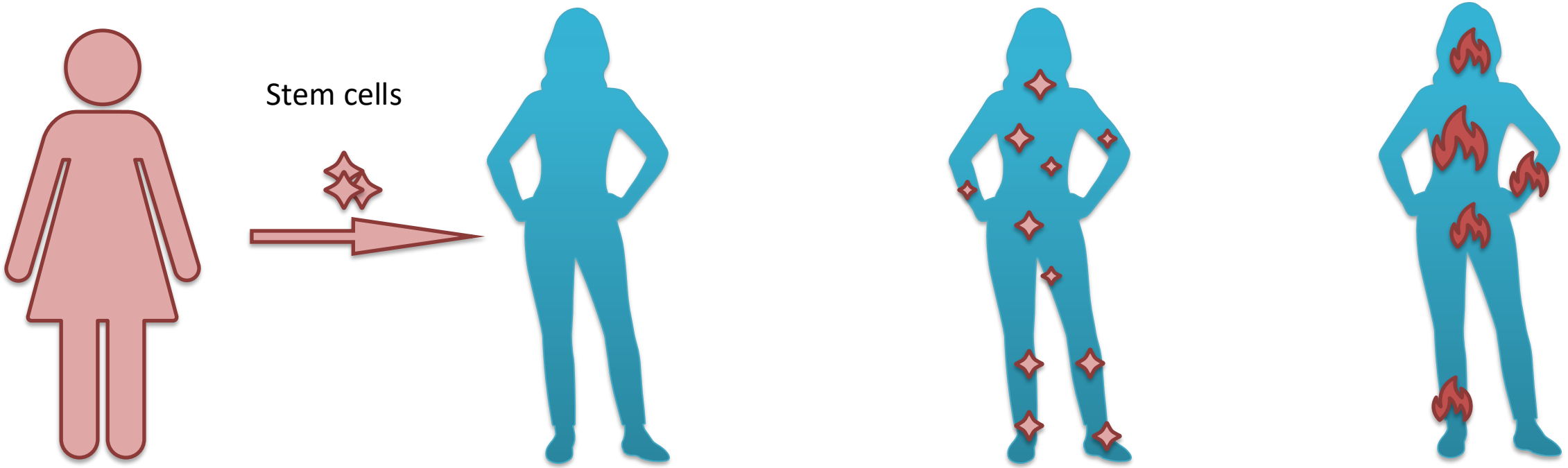
Oil glands damage

Surface damage

Not able to heal !

Would It Go Away?

- the most common question I get



So far, we can manage, but can't get rid of it.

Avoid Harm

- Avoid harmful behavior
  - Do not wear regular contact lens
  - Do not rub your eyes (this is for everybody!)
  - Do not dig for mucous or scratch the crusting with nails
  - Do not use redness reliever such as Visine, Opcon A, Naphcon A, Cleareyes
  - Do not use allergy eye drop such as Allaway, Zaditor
  - Do not wear contact lenses
- Decrease screen time, take breaks
- Be very careful with makeup and makeup removal

The Eye Makes Mucous Due to Inflammation

- Not infectious conjunctivitis
- Antibiotics don’t really work
- Visine is TOXIC!

Control the Environment

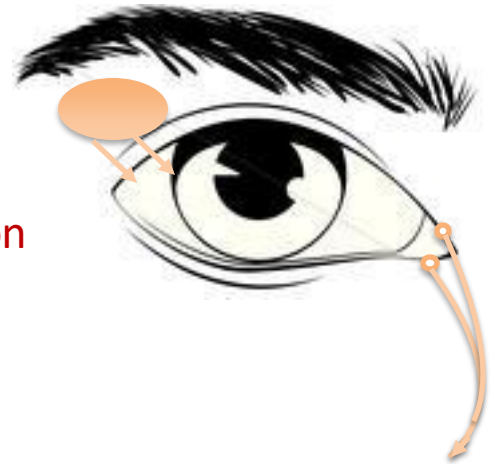
- Modify environmental factors
  - Point air vents in the car away from your face
  - Humidifier ON! all the time when heat is on
  - Wear sunglasses
  - Sports goggles (for motorcycling) available to create “moisture chambers”

- Warm compress (without lid scrubs)

Keep The Eyes Wet

Dryness

Tear production



Tear drainage

1. Lubricate very frequently
2. Make more tears (hard to do)
3. Control the environmental humidity
4. Punctal occlusion

Preservative-Free Lubricant

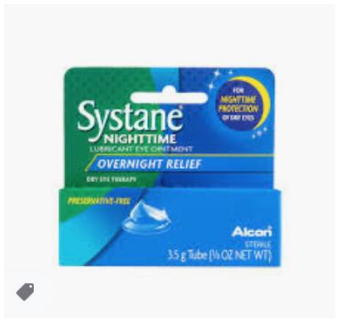
Preservative-Free Lubricant

- The correct frequency is to keep symptoms at minimum in between the drops
- One drop at a time is enough
- Recapping or not

Lubricant Ointment at Night

Lubricant Eye Ointment ...
amazon.com

Amazon.com : Systane Nightti...
amazon.com



SYSTANE Lubricant Eye Ointme...
walmart.com · In stock

Lubricant Eye Ointment, 0.12 O...
cvs.com

Refresh Lacri-Lube Lubricant E...
walgreens.com · In stock

Amazon.com: PACK OF 3 - Systa...
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Systane GEL Lubricant Eye G...
heb.com · In stock

Refresh Lacri-Lube Lub...
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Bausch & Lomb Lubricant Ey...
riteaid.com · In stock

Genteal Lubricant Eye Ointment – Dry...
dryeyeshop.com · In stock

Alcon Systane Nighttime Lubrica...
ebay.com

Refresh PM Lubricating eye ointmen...
dryeyeshop.com · In stock

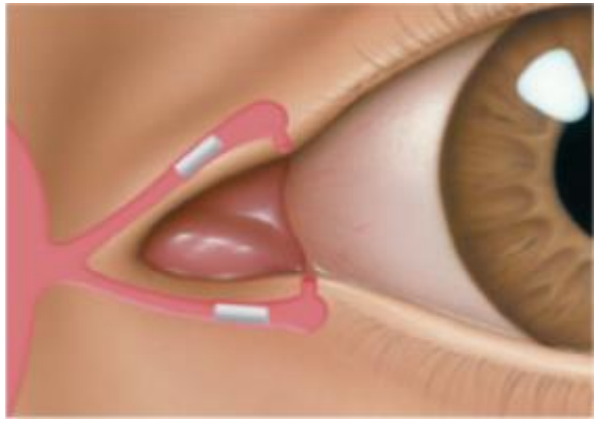
preservative-free

Make More Tears

- Artificial tears (*preservative-free*)
- ReStasis and/or Xiidra
  - seem to work only in very mild cases
  - early start (prior to transplant) may have some benefit
  - not helpful in late stages
- Oral Pilocarpine (Salagen) or Cevimeline (Evoxac)
  - Often Rx for dry mouth
  - Induce tear production as well
  - Side effects can be moderated by careful titration in many cases

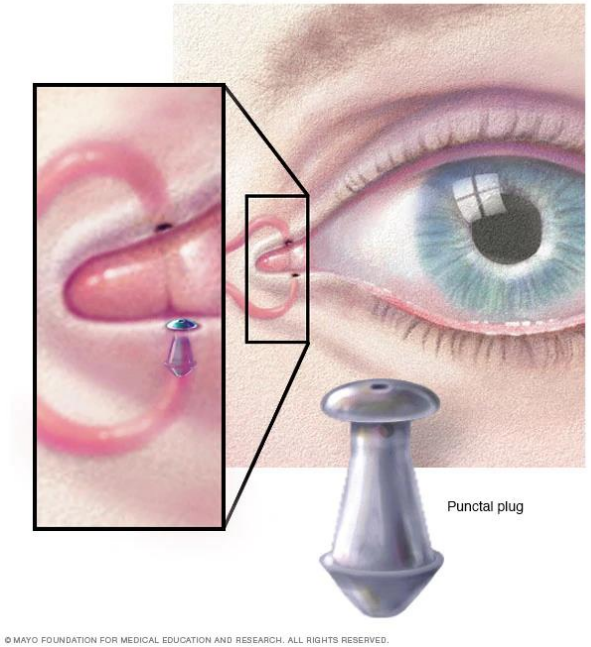
Punctal Occlusion - Close the Drains

Dissolvable or non-dissolvable



Jehangir N et al. Journal of Ophthalmology 2016

Permanent - silicone



Punctal cautery works the best

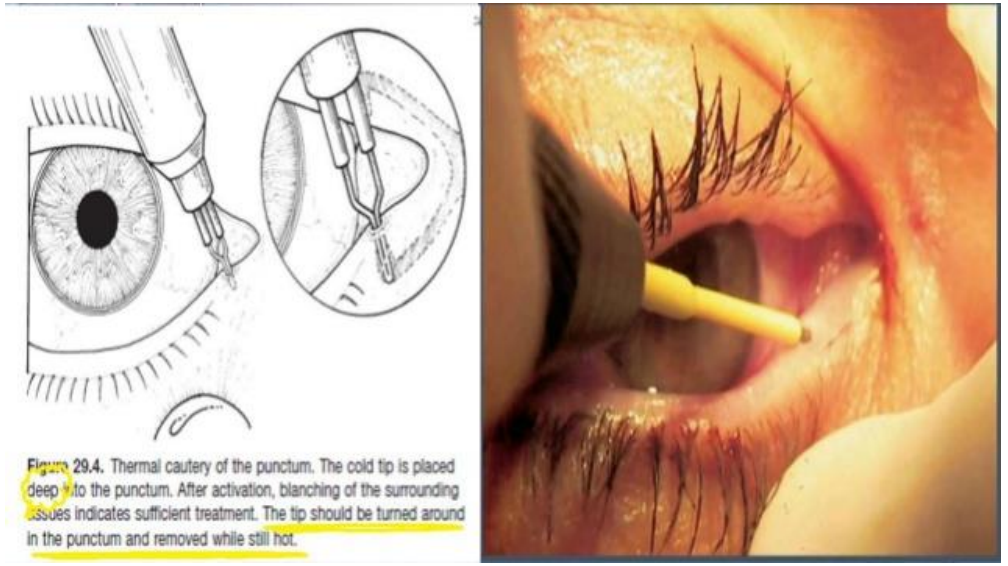


Figure 29.4. Thermal cautery of the punctum. The cold tip is placed deep into the punctum. After activation, blanching of the surrounding tissues indicates sufficient treatment. The tip should be turned around in the punctum and removed while still hot.

Marjan Mazouchi. Health & Medicine 2019

Control the Inflammation

- Systemic immunosuppression and GvHD treatment
  - oral steroids, tacrolimus, and many other systemic treatments
  - Managed by your transplant doctor, works on the whole body
  - watch out during taper!
- Topical steroids (appropriate taper and close monitoring)
  - If a steroid eye medication is prescribed, follow-up is a must
  - Steroid strength
  - Effects on eye pressure
  - Preservative-free version of steroids

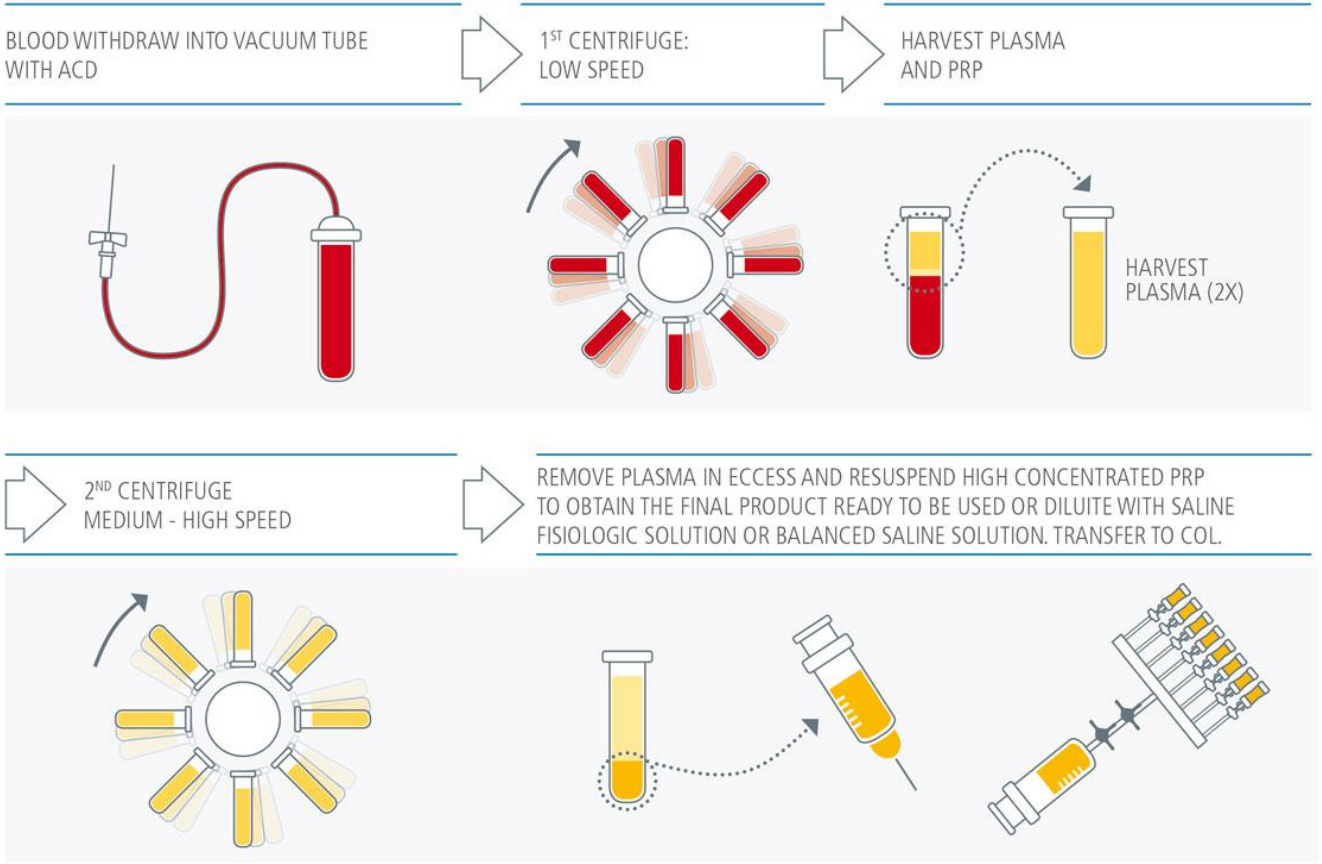
Inflammation

Surface damage

Redness

Give the Eyes Nutrition

- Serum tears (from your own blood)
  - labor intensive but often works well
  - Blood draw every couple of months



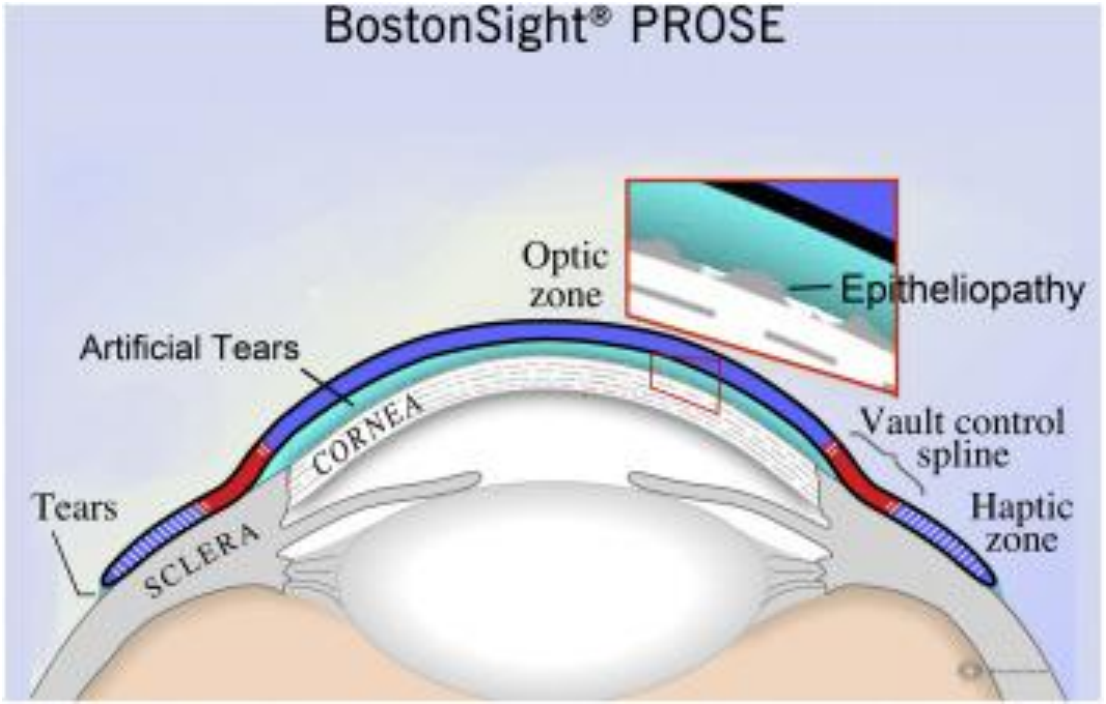
The entire process of PRP preparation should be carried out in a clean and sterile place with aseptic technique.

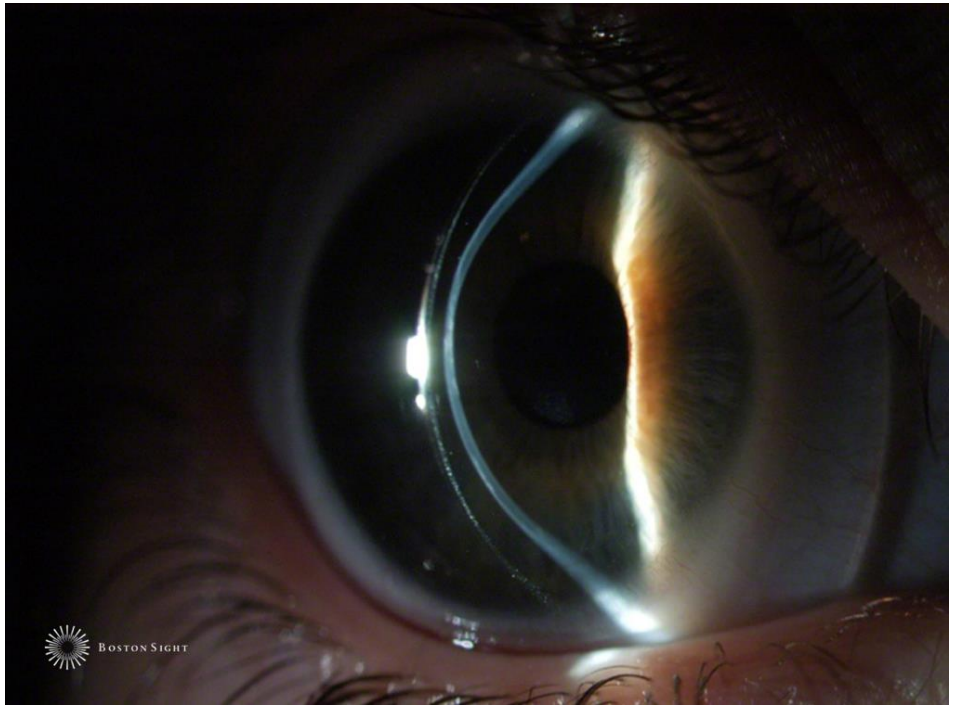
http://www.biomeddevice.it/index.php/en/ophtalmology

Therapeutic Scleral Lens

1. These are NOT regular soft or hard contact lens
2. They are fitted only by an optometrist who had special residency training
3. Your transplant doctor or GvHD eye doctor's referral is needed
4. High cost, poor insurance coverage, steep learning curve, but life-changing result for many
5. Major ones are:
   - Boston Sight (www.bostonsight.org)
   - GP lens Institute (www.gpli.info)
   - EyePrintPro (www.eyeprintpro.com)

BostonSight PROSE





Surgical Treatments

1. The goal is to avoid having to do surgery if possible
   - corneal patch or transplant is NOT curative and is harder to take care of in the long run
   - amniotic membrane helps with healing but will not melt in days or weeks
   - none are comfortable

2. Avoid cosmetic eyelid surgery, eyeliner tattoo, lash extension, or laser vision correction
   - any tissue damage can increase inflammation
   - lid surgery and LASIK worsen dry eyes

3. Cataract surgery is an exception; it is necessary but needs to be done with extreme care
   - go to a surgeon with experience in oGvHD
   - pre-op and post-op care different from general population

Support the Research Efforts

- More than a dozen trials in the US to date
- Completed/terminated/withdrawn - recruitment issue
- None FDA approved for ocular GVHD

What You Can and Should Do?

- Recognize eye symptoms
  - You are overwhelmed, tired, hurt, and fed up!
  - However, nobody knows how your eyes feel before and after
  - Remember, early diagnosis and treatment make a difference in outcome
  - Avoid getting to the point of no return

What You and Your Family Can Do?

- Advocate for diagnosis and treatment
  - request inpatient consult if needed
  - volunteer information to your transplant doctor about your eyes
  - ask for a referral to an eye doctor experienced in GvHD before and after transplant
  - discuss any eye treatment or procedure and systemic treatment change with the specialist

What Can Your Eye Doctors Do?

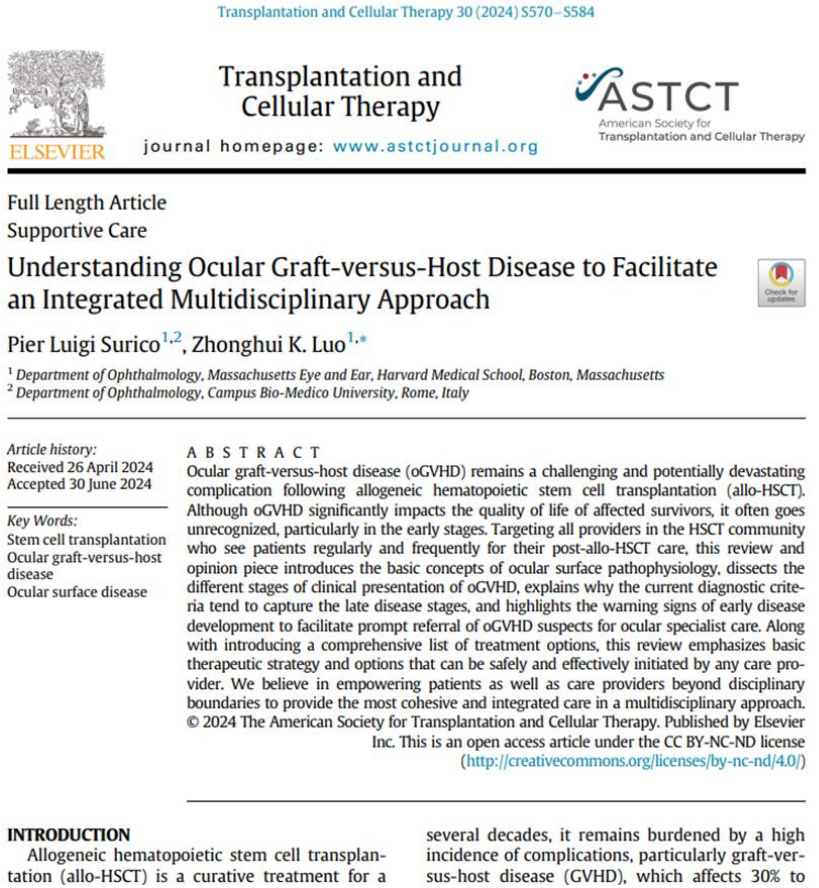
- Look for signs of ocular GvHD vs. other eye problems
- If you have a local eye doctor (general ophthalmologist or optometrist)
  - co-manage with specialist experienced in oGvHD
  - It is NOT just dry eyes!
  - It can rapidly progress into serious and irreversible situations!
- Initiate treatments as discussed earlier
- Promote the communication between all your doctors
  - Transplant service, dermatology, oral medicine, oncologist, PCP, everybody!

It is “We” and “Us” working together!

First, understand the problems

Second, avoid preventable damage

Third, invest (commit) in management



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Full Length Article
Supportive Care

Understanding Ocular Graft-versus-Host Disease to Facilitate an Integrated Multidisciplinary Approach

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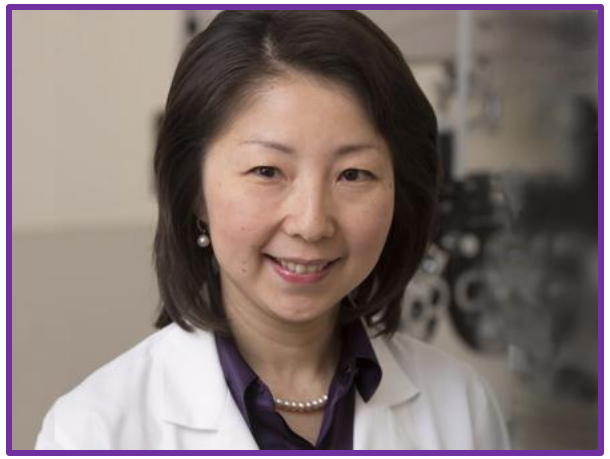
A B S T R A C T

Ocular graft-versus-host disease (oGVHD) remains a challenging and potentially devastating complication following allogeneic hematopoietic stem cell transplantation (allo-HSCT). Although oGVHD significantly impacts the quality of life of affected survivors, it often goes unrecognized, particularly in the early stages. Targeting all providers in the HSCT community who see patients regularly and frequently for their post-allo-HSCT care, this review and opinion piece introduces the basic concepts of ocular surface pathophysiology, dissects the different stages of clinical presentation of oGVHD, explains why the current diagnostic criteria tend to capture the late disease stages, and highlights the warning signs of early disease development to facilitate prompt referral of oGVHD suspects for ocular specialist care. Along with introducing a comprehensive list of treatment options, this review emphasizes basic therapeutic strategy and options that can be safely and effectively initiated by any care provider. We believe in empowering patients as well as care providers beyond disciplinary boundaries to provide the most cohesive and integrated care in a multidisciplinary approach.

INTRODUCTION

Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is a curative treatment for a several decades, it remains burdened by a high incidence of complications, particularly graft-versus-host disease (GVHD), which affects 30% to

Questions?



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