

Graft-versus-Host Disease: Eyes

Celebrating a Second Chance at Life Survivorship Symposium

April 29 – May 5, 2023



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FINANCIAL DISCLOSURES

No relevant disclosures

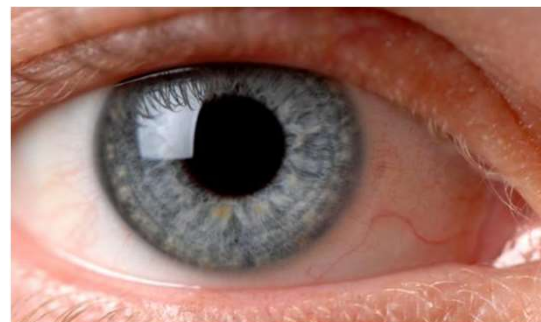
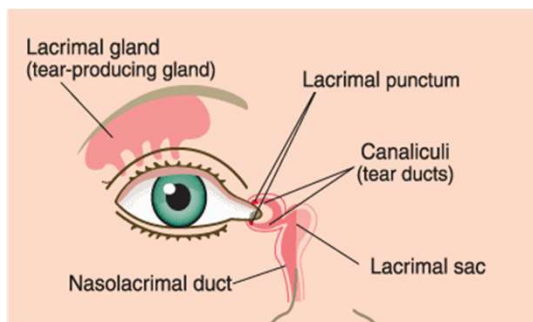
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INCIDENCE

- Incidence of ocular GVHD varies widely among studies (10-90%)
- More recent study showed 40-60%
- If patients already have other chronic graft-versus-host disease, 60-90% will have ocular GVHD
 - Only 9% acute ocular GVHD
- Ocular GVHD may be the first affected organ
 - 22% of new onset dry eye patients after HSCT presented with dry eye and conjunctival inflammation without features of systemic GVHD

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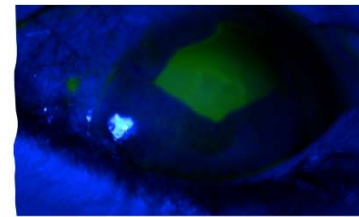
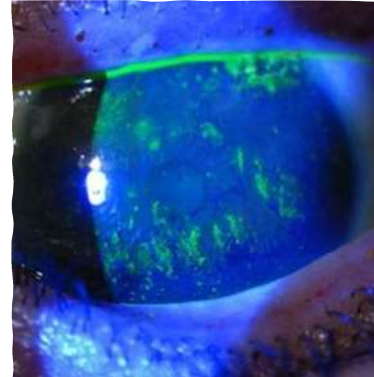
CLINICAL PRESENTATION: OCULAR SURFACE



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CLINICAL PRESENTATION: All layers of the eye

- Eyelids: Meibomian gland dysfunction, spontaneous punctal occlusion, cicatricial entropion or ectropion
- Conjunctiva: conjunctivitis, membranous or pseudomembranous
- Cornea: filamentary keratitis, epithelial defects, descemetocele, perforation
- Lacrimal gland dysfunction
- Uvea: uveitis, posterior synechiae



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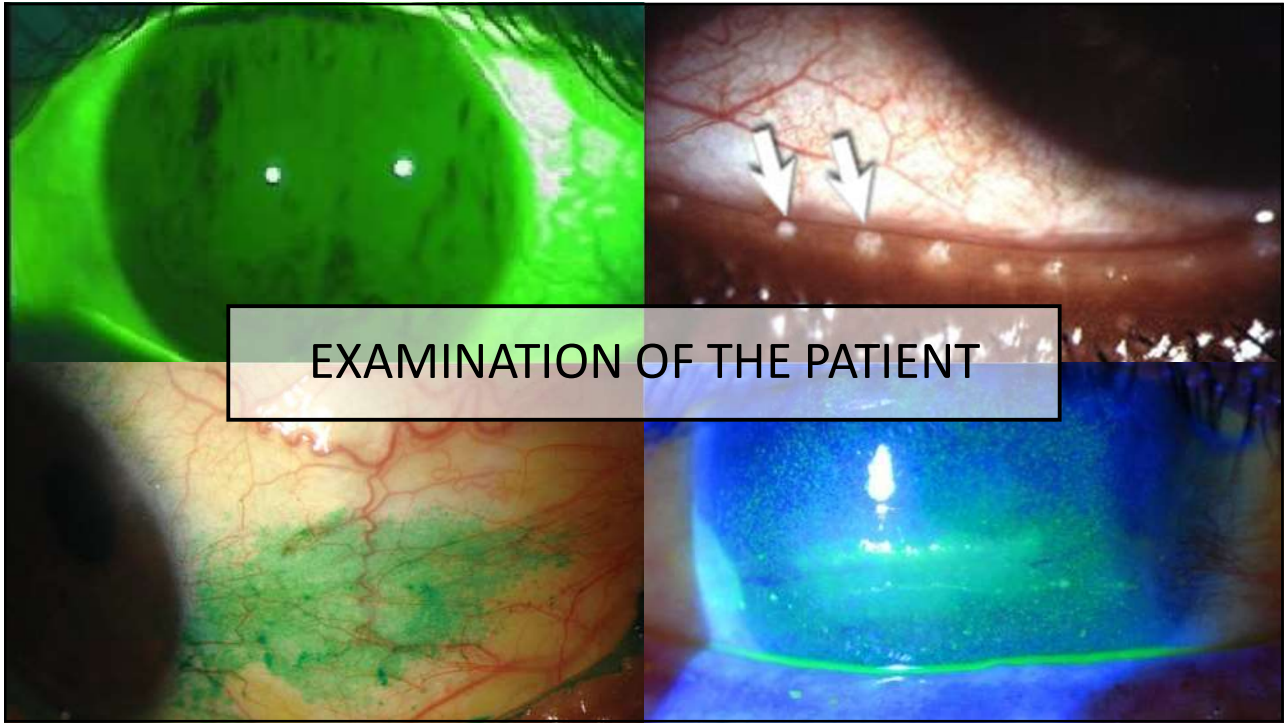
BURDEN OF DISEASE

- Impact of **severe** dry eye on a patient's life:
- Comparable to moderate to severe chest pain
- For the **most severe** dry eye cases:
- Thought to be worse than a disabling hip fracture



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DRY EYE TESTING

OS	
Average LLT	85 nm
Partial Blinks	6 / 8
C-Factor	0.71

Lipid Thickness (nm)

100
75
50
25
0

0 2 4 6 8 10 12 14 16 18 20

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ACUTE GVHD STAGING

The Eye in Bone Marrow Transplantation

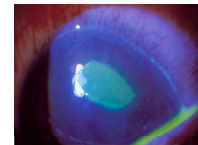
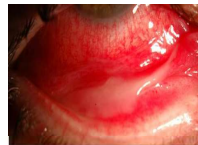
III. Conjunctival Graft-vs-Host Disease

Table 4.—Proposed Clinical Staging of Conjunctival GVHD*

Stage	Description
1	Conjunctival hyperemia
2	Conjunctival hyperemia with chemotic response or serosanguineous exudate
3	Pseudomembranous conjunctivitis
4	Pseudomembranous conjunctivitis plus corneal epithelial slough

* GVHD indicates graft-vs-host disease.

Arch Ophthalmology Sept 1989



CHRONIC GVHD STAGING

National Institutes of Health Consensus Development Project on Criteria for Clinical Trials in Chronic Graft-versus-Host Disease:

I. The 2014 Diagnosis and Staging Working Group Report

	SCORE 0	SCORE 1	SCORE 2	SCORE 3
EYES	No symptoms	Mild dry eye symptoms not affecting ADL	Moderate dry eye symptoms partially affecting ADL	Severe dry eye symptoms significantly affecting ADL
<i>Keratoconjunctivitis sicca (KCS) confirmed by ophthalmologist:</i>		(requirement of lubricant eye drops ≤ 3 x per day)	(requiring lubricant eye drops > 3 x per day or punctal plugs),	(special eyewear to relieve pain)
Yes			WITHOUT new vision impairment due to KCS	OR unable to work because of ocular symptoms OR loss of vision due to KCS
No				
Not examined				

CHRONIC GVHD CONSENSUS: BACKGROUND

- International chronic ocular graft-vs-host disease consensus group held four working meetings in 2013
- Scored different variables to assign patients to three diagnostic categories: No, probable, and definite GVHD
- In 2022, there was a multicenter prospective validation study compared to NIH diagnostic criteria from 2014
- Good sensitivity, specificity, predictive value and correlation between the two studies

Scientific Reports May 2013
The Ocular surface 2022



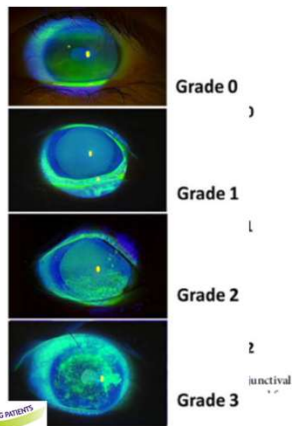
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CHRONIC GVHD CONSENSUS: GRADING

CORNEAL FLUORESCHEIN STAINING

CONJUNCTIVAL INJECTION SCORE



Scientific Reports May 2013



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CHRONIC GVHD CONSENSUS: QUESTIONNAIRE

Scientific Reports May 2013



OSDI (Ocular Surface Disease Index)

Patient name: _____ Date of birth: _____ Patient ID: _____

Have you experienced any of the following during the last week?

	All of the time	Most of the time	Half of the time	Some of the time	None of the time
1. Eyes that are sensitive to light?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2. Eyes that feel gritty?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3. Painful or sore eyes?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
4. Blurred vision?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
5. Poor vision?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Have you problems with your eyes limited you in performance any of the following during the last week?

	All of the time	Most of the time	Half of the time	Some of the time	None of the time	No Answer
6. Reading?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
7. Driving at night?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
8. Working with a computer or bank machine (ATM)?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
9. Watching TV?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Have your eyes felt uncomfortable in any of the following situations during last week?

	All of the time	Most of the time	Half of the time	Some of the time	None of the time	No Answer
10. Windy conditions?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
11. Places or areas with low humidity (very dry)?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
12. Areas that are air conditioned?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

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CHRONIC GVHD CONSENSUS: SCALE

International Chronic Ocular Graft-vs-Host-Disease (GVHD) Consensus Group: Proposed Diagnostic Criteria for Chronic GVHD (Part I)

Yoko Ogawa¹, Stella K. Kim², Reza Dana³, Janine Clayton⁴, Sandeep Jain⁵, Mark L. Rosenblatt⁶, Victor L. Perez⁷, Hasanain Shikari⁸, Anjo Riemens⁹ & Kazuo Tsubota¹

Table 1 | Severity scale in chronic ocular GVHD

Severity scores (points)	Schimer's test (mm)	CFS (points)	OSDI (points)	Conj (points)
0	>15	0	<13	None
1	11-15	<2	13-22	Mild/Moderate
2	6-10	2-3	23-32	Severe
3	≤5	≥4	≥33	

CFS; corneal fluorescein staining, OSDI; Ocular Surface Disease Index, Conj; conjunctival injection. Severity classification; Total score (points); (Schimer's test score+ CFS score+ OSDI score+ Conj injection score) = None, 0-4, Mild/Moderate; 5-8, Severe, 9-11.

Table 2 | Diagnosis of chronic ocular GVHD

	None (points)	Probable GVHD (points)	Definite GVHD (points)
Systemic GVHD(-)	0-5	6-7	≥8
Systemic GVHD(+)	0-3	4-5	≥6

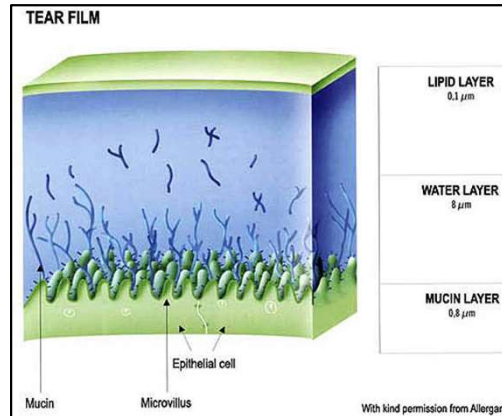
Scientific Reports May 2013



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TEAR COMPOSITION



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TREATMENT GOALS

- Ocular management:
 - First try organ specific treatments
 - Instead of just increasing systemic immunosuppression
- Three ocular goals:
 - Lubrication of the ocular surface
 - Control evaporation
 - Decrease ocular surface inflammation



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TREATMENTS

Lubrication

- Artificial Tears, gels, ointments
- Moisture Goggles
- Punctal occlusion (plug, cautery)
- Cyclosporine, lifitegrast
- Serum Tears
- Scleral lenses

Control evaporation

- Warm Compresses
- Lid Hygiene
- Topical antibiotic (Azithromycin)
- Oral antibiotic (Doxycycline)
- Lid procedures (Blephex, Lipiflow, IPL)

Decrease inflammation

- Corticosteroids
- Topical cyclosporine, lifitegrast

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LUBRICATION

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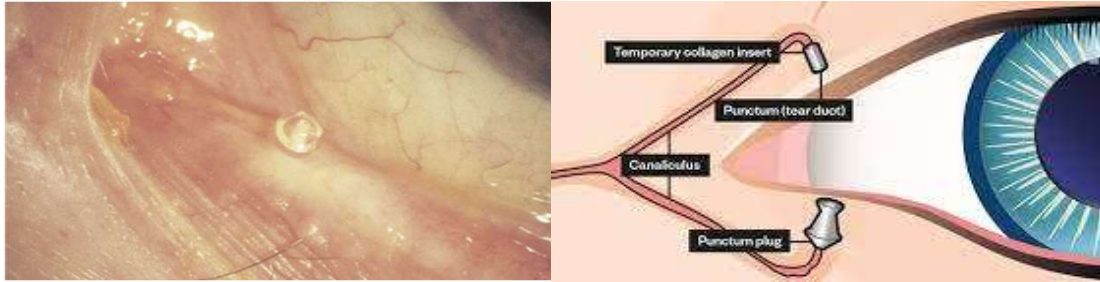
ARTIFICIAL TEARS



NIGHTTIME LUBRICATION



PUNCTAL PLUGS



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CYCLOSPORINE & LIFITEGRAST

- Different formulations:
 - Restasis 0.05%
 - Cequa 0.09%
 - Xiidra 5%
- Can take time to reach peak efficacy
- Work to increase tear production and decrease inflammation

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SERUM TEARS



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SCLERAL LENSES

- Rigid gas permeable scleral prosthetic device
- Fluid-ventilated with artificial tears
- Liquid corneal bandage
- Re-establishes a healthy stable ocular surface environment
- Mitigates pain and photophobia



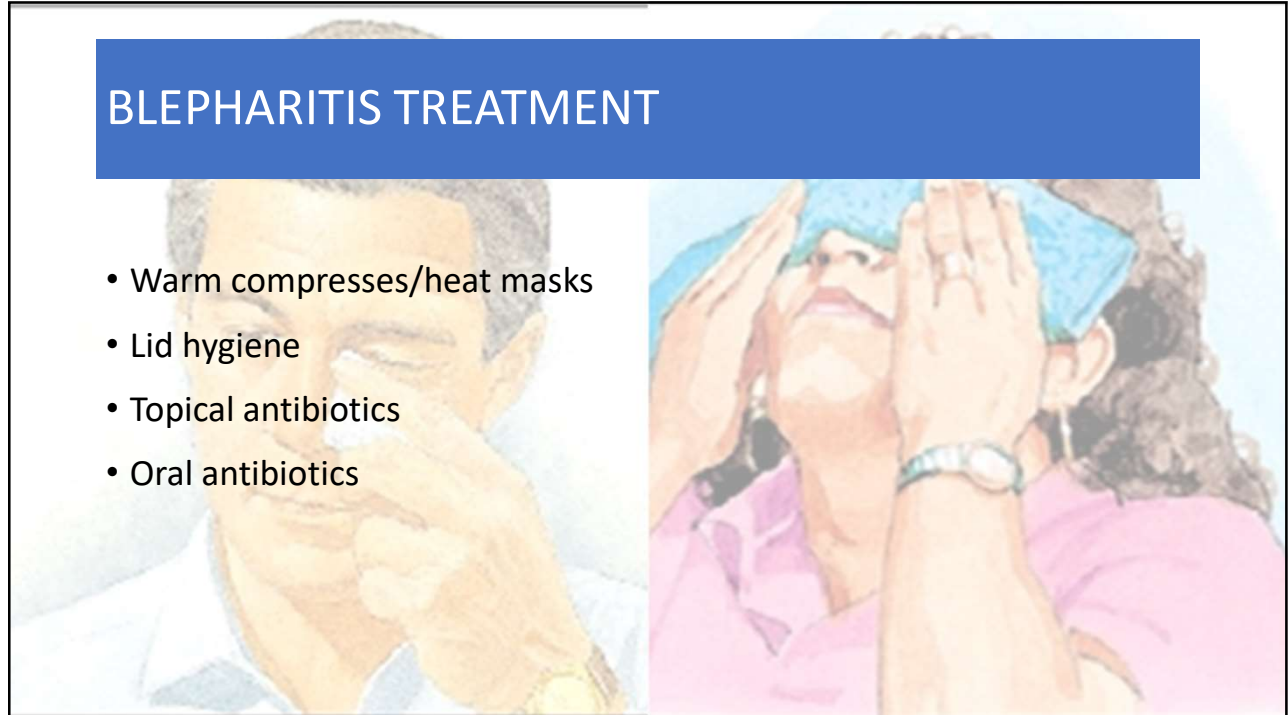
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CONTROL EVAPORATION

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BLEPHARITIS TREATMENT

- Warm compresses/heat masks
- Lid hygiene
- Topical antibiotics
- Oral antibiotics



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EYELID PROCEDURES



DECREASE INFLAMMATION

TOPICAL CORTICOSTEROIDS

- Pulsed therapy
- Not a good long-term option
- Increases risk of both:
 - Cataracts
 - Glaucoma

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SURGICAL OPTIONS

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SURGICAL GOALS

- When conventional medical therapy fails
 - Surgical interventions should be considered
- Goals:
 - Increase lubrication
 - Assist epithelialization
 - Remove corneal opacities
 - Restore vision

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TARSORRHAPHY



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AMNIOTIC MEMBRANE

- Amniotic membrane is derived from inner layer of the placenta
 - Avascular connective tissue
- Promotes re-epithelialization
- Decreases inflammation and fibrosis
- Serves as biologic bandage



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CORNEAL TRANSPLANTATION

- Need to optimize ocular surface prior to transplantation
- May need to combine with limbal stem cell transplant, amniotic membrane, bandage contact lens or tarsorrhaphy
 - Maximize tear function
 - Restore normal lid anatomy and function



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TIMING OF TREATMENT

- **Unclear**

- Pre-BMT initiation of topical cyclosporine may reduce the inflammatory response in the lacrimal glands and improve dry eye

- **Mian et al 2010: 105 patient retrospective review**

- 81 patients received topical Cyclosporine 1 month prior to BMT
- 24 patients did not receive Cyclosporine til at least 6 months after BMT
- Dry eye symptoms were significantly more severe in control group at 3 months, 1 year and 2 years

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SUMMARY



Ocular GVHD can lead to disabling pain and blindness



Early detection, diagnosis and treatment are key to prevent long-term complications



Evaluate all patients as early as possible, possibly even pre-transplant if feasible.

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QUESTIONS?



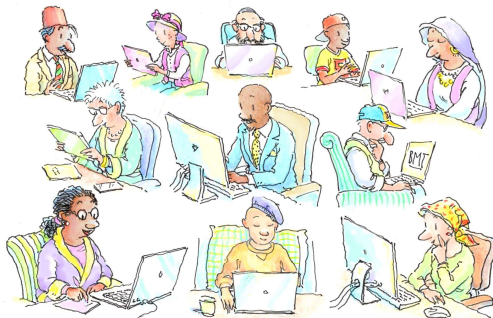
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