

The quest for perfection in the Ocular Surface

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Structure and Function of the Ocular Surface

- Complex interactions exist between the **three main structures** of the ocular surface:
 - Cornea
 - Conjunctiva
 - Tear film
- The ocular surface is a functional unit that:
 - **Maintains** the integrity of the cornea
 - **Preserves** the quality of the refractive surface of the eye and, thus, visual function
 - **Resists** injury and protects the eye against environmental conditions

1. Pauly A, et al. *IOVS* 2007;48(12):5473-83.
2. Rolando M, Zierhut M. *Surv Ophthalmol* 2001;45 Suppl 2:S203-10.

Definition and Common Causes of OSD

- Ocular surface disease (OSD) includes any condition that:
 - Leads to a dysfunctional tear film
 - May cause noticeable irritation to the front of the eye and degradation of vision
- OSD is related to structural or functional problems of the eyelids, cornea or conjunctiva
- Common forms of OSD include:
 - Blepharitis (inflammation of the eyelids)
 - Tear film dysfunctions (e.g. dry eye disease)
 - Sjögrens syndrome
 - Meibomian gland dysfunction

1. Rolando et al. *Br J Ophthalmol* 2010;94(Suppl1):i1-9.
2. Lemp MA. *Ocul Surf* 2007;5(2):69-204.

Impact of Ocular Surface Disease on Visual Acuity and Contrast Sensitivity

- The tear film provides the greatest optical power of any ocular surface and is essential for good quality vision
- Corneal surface irregularity due to epithelial desiccation can lead to decreased visual acuity
- Decreases in spatial contrast sensitivity ranged from 35% to 70% in patients with dry eye disease, compared with normal eyes³
 - Evidence indicates that decreased spatial contrast sensitivity correlates with loss of visual acuity in patients with dry eye

1. Albarrán C, et al. *Cont Lens Anterior Eye* 1997;20(4):129-35.

2. Vitale S, et al. *Health Qual Life Outcomes* 2004;2:44.

3. de Paiva CS, et al. *Ophthalmol* 2003;110(6):1102-9.

4. Rolando M, et al. *Cornea* 1998;17(4):376-9.

Impact of OSD on Vision-Related Quality of Life

- Impaired visual acuity, contrast sensitivity, and visual function can have a profound effect on vision-related quality of life
- Dry eye disease decreases the quality of patients' lives and their ability to perform daily functions

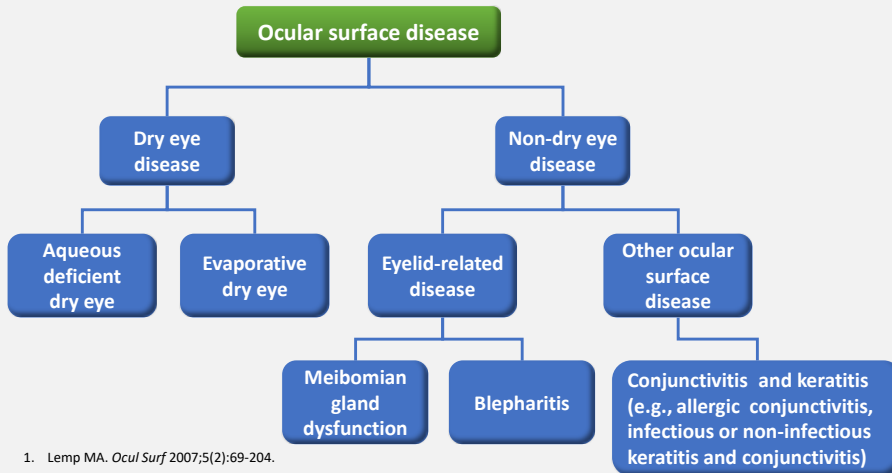
Daily Life Function	Patients Reporting Interference (%)
Night time driving	32.3
Reading	27.5
Computer work	25.7
Watching television	17.9

1. Lemp MA. *Ocul Surf* 2007;5(2):69-204.

2. Goto E, et al. *Am J Ophthalmol* 2002;133(2):181-6.

3. Montes-Mico R, et al. *IOVS* 2005;46(5):1615-9.

Association Between OSD and Dry Eye Disease



Dry eye disease



Dry eye disease is defined as a multifactorial disease of the ocular surface and tear film that results in symptoms of discomfort, visual disturbance and tear film instability

It is characterized by **hyperosmolarity** of the tear film and **inflammation** of the ocular surface



Management of OSD is based on careful clinical observation and accurate diagnosis of the underlying causative factors

Identify the problem

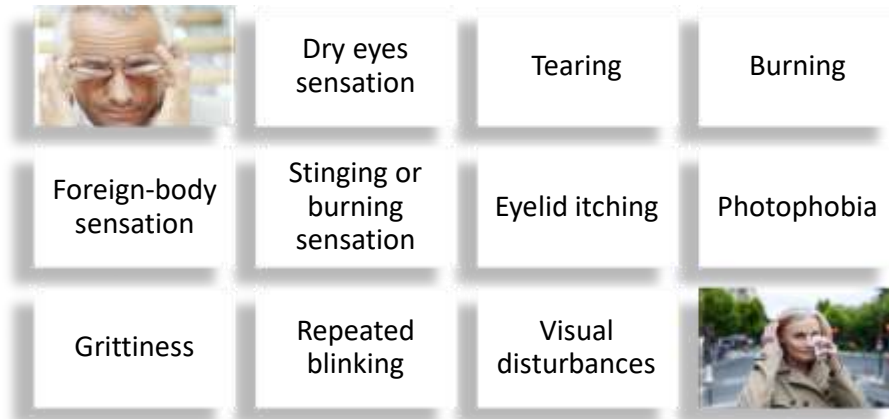


Ask for symptoms of OSD



Slit-lamp examination can be used to examine the eyelids, margins, glands, and the ocular surface

Symptoms of OSD



Questionnaire: Ocular Surface Disease Index (OSDI)

- A set of 12 questions
- Used as a measure of outcome in randomised controlled trials
- Scores on scale (grading from 0 to 4)
- OSDI score = $[(\text{sum of the scores for all questions answered}) \times 100] / [(\text{total number of questions answered}) \times 4]$
- Assessment: Scale of 0–100¹
 - Higher the score more severe the disease
- Advantage: OSDI is a valid and reliable instrument for measuring the severity of Dry Eye disease

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?	4	3	2	1	0
2. Eyes that feel gritty?	4	3	2	1	0
3. Painful or sore eyes?	4	3	2	1	0
4. Blurred vision?	4	3	2	1	0
5. Poor vision?	4	3	2	1	0

Subtotal score for answers 1 to 5 (A)

Have problems with your eyes limited you in performing 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	NOT Applicable
6. Reading?	4	3	2	1	0	N/A
7. Driving at night?	4	3	2	1	0	N/A
8. Working with a computer or bank machine (ATM)?	4	3	2	1	0	N/A
9. Watching TV?	4	3	2	1	0	N/A

Subtotal score for answers 6 to 9 (B)

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

	All of the time	Most of the time	Half of the time	Some of the time	None of the time	Not Applicable
10. Windy conditions?	4	3	2	1	0	N/A
11. Places or areas with low humidity (very ...)?	4	3	2	1	0	N/A
12. Areas that are air conditioned?	4	3	2	1	0	N/A

Subtotal score for answers 10 to 12 (C)

The epidemiology of dry eye disease: report of the epidemiology subcommittee of the international dry eye workshop. Ocul Surf 2007 Apr;5(2):93-107.
Schiffman RM, Christianson MD, Jacobsen G, Hirsch JD, Reis BL. Reliability and validity of the ocular surface disease index. Arch Ophthalmol 2000 May;118(5):615-21.
Perry HD, Donnenfeld ED. Dry eye diagnosis and management in 2004. Curr Opin Ophthalmol 2004 Aug;15(4):299-304.

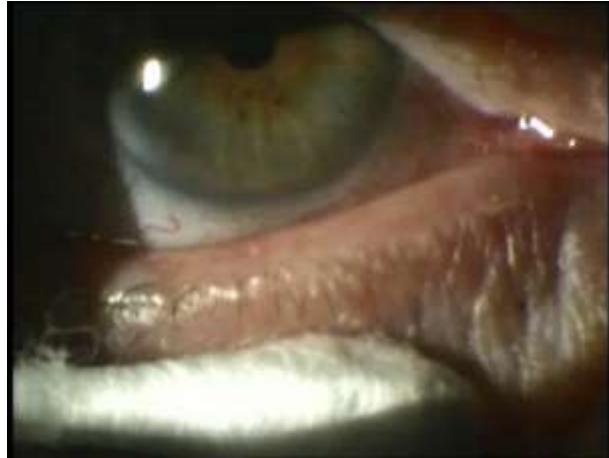
Common Signs of OSD

- ✓ Abnormal Schirmer test
- ✓ Abnormal tear break-up time test (TBUT)
- ✓ Corneal and/or conjunctival staining
- ✓ Meibomian gland dysfunction
- ✓ Lid margin vascularization
- ✓ Lid margin laxity and/or irregularity

Delayed Clearance Loose interface – Floppy eyelid



Lower eyelid horizontal laxity



Lid margin changes - MGD



Lid margin hyperemia
orifice opacity with plugging



Lid margin hyperemia
orifice opacity with plugging



Orifices open onto the
marginal conjunctiva



Orifice opacification with
periductal fibrosis



Epithelial ridging
between opacified MG

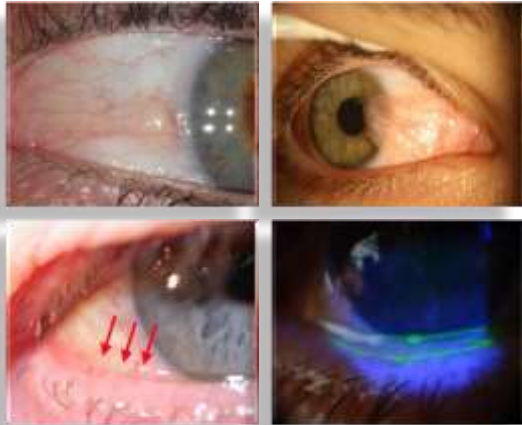


Notching of posterior lid margin
tissue absorption of the orifices

Ineffective tear spread

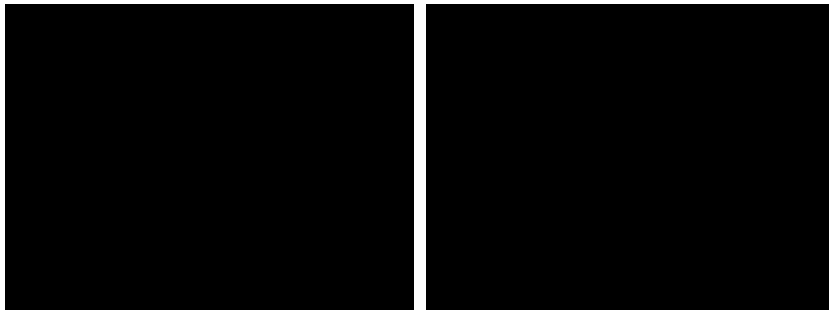
Ocular Surface irregularity

- Dellen
- Pingueculae
- Pterygium
- Conjunctivochalasis

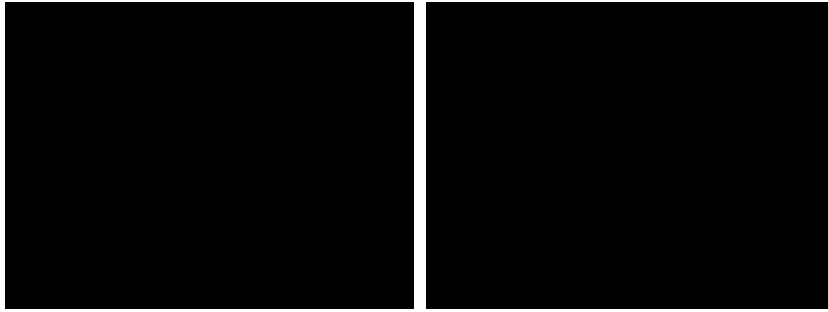


Tseng SC. A practical treatment algorithm for managing ocular surface and tear disorders. Cornea. 2011

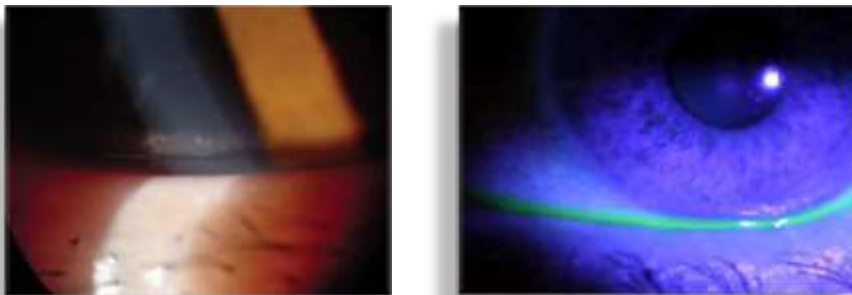
Blepharitis-MGD



Lipid layer deficiency



Tear Meniscus Height



Tear meniscus height: <0.35 mm

Schirmer's Test



≤3 mm: Confirmed diagnosis of an aqueous-deficient eye
≤5 mm: Highly probable diagnosis of an aqueous-deficient eye
6 to 10 mm: Marginal or grey zone of aqueous deficiency

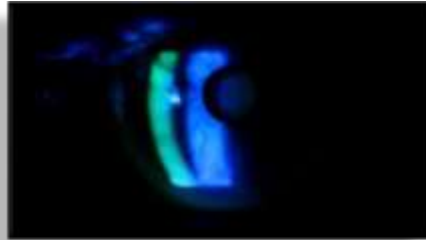
TBUT Test



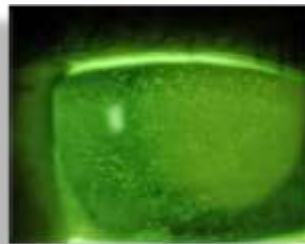
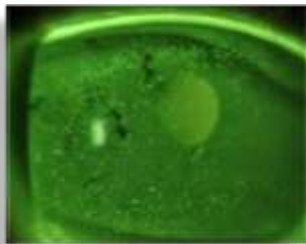
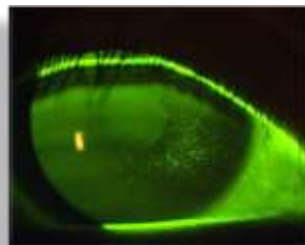
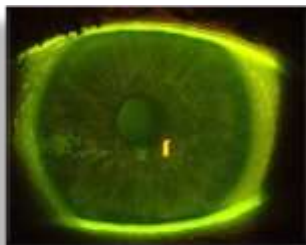
Normal: >10 sec,
Dry Eye ≤10 sec

Ocular surface staining

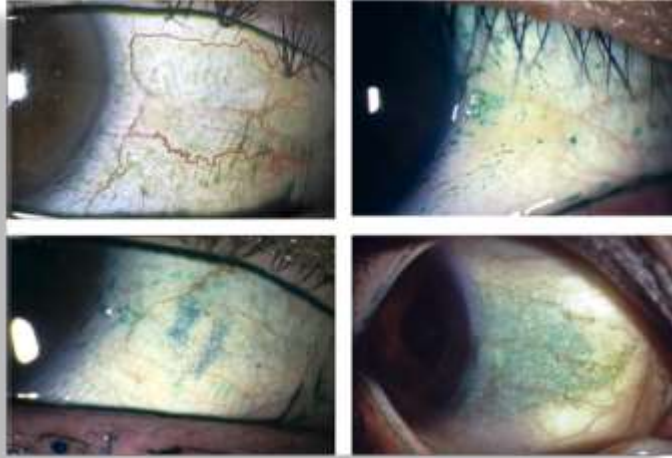
	Fluorescein	Lissamine green
Staining of healthy cells	×	×
Staining of dead cells	×	✓
Blocked by mucin	×	×
Intrinsic toxicity	×	✓
Phototoxicity	×	Not done
Stromal diffusion	Fastest	Fast
Staining promoted by	Cell-cell junction disruption	Cell-cell junction disruption or cell death



Fluorescein Staining

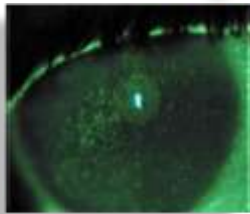


Lissamine green Staining



John P. Whitcher et al. American Journal of Ophthalmology 2010

Grading of corneal and conjunctival staining Oxford Scheme



PANEL		Grade
A		0
B		I
C		II
D		III
E		IV
>E		V

Bron AJ. Grading of corneal and conjunctival staining in the context of other dry eye tests. Cornea. 2003

Meibomian Gland Expression



Osmolarity Measure

- Hyperosmolarity is a well-established fundamental characteristic of dry eye disease
- The osmolarity test assists clinicians in making a rapid differential diagnosis



MMP-9 test

- MMP-9 is produced by the entire lacrimal system
- Reliable biomarker for inflammation, consistently elevated in the tears of patients with OSD



InflammaDry limit of detection

Literature meta-analysis supports that normal levels of MMP-9 in human controls range from 3-41 ng/ml¹⁻⁷

POSITIVE TEST RESULT

MMP-9 \geq 40 ng/ml



NEGATIVE TEST RESULT

MMP-9 < 40 ng/ml



[1] Acera A, Rocha G, Vecino E, et al. Inflammatory markers in the tears of patients with ocular surface disease. *Ophthalmic Res.* 2008 Oct; 40(6):315-21.
 [2] Chotikavanich S, de Paiva CS, Li de Q, et al. Production and activity of matrix metalloproteinase-9 on the ocular surface increase in dysfunctional tear syndrome. *Invest Ophthalmol Vis Sci.* 2009 Jul; 50(7):3203-9.
 [3] Solomon A, Dursun D, Liu Z, et al. Pro- and anti-inflammatory forms of interleukin-1 in the tear fluid and conjunctiva of patients with dry-eye disease. *Invest Ophthalmol Vis Sci.* 2001;42(10):2283-92.
 [4] Leonardi A, Brun P, Abatangelo G, et al. Tear levels and activity of matrix metalloproteinase (MMP)-1 and MMP-9 in vernal keratoconjunctivitis. *Invest Ophthalmol Vis Sci.* 2003;44(7):3052-8.
 [5] Lema I, Sobrino T, Durán JA, et al. Subclinical keratoconus and inflammatory molecules from tears. *Br J Ophthalmol.* 2009;93(6):820-4.
 [6] Honda N, Miyai T, Nejima R, et al. Effect of latanoprost on the expression of matrix metalloproteinases and tissue inhibitor of metalloproteinase 1 on the ocular surface. *Arch Ophthalmol.* 2010;128(4):466-71.
 [7] Markoulli M, Papas E, Cole N, et al. The effect of contact lens wear on the diurnal profile of matrix metalloproteinase-9 and its inhibitor in the tear film. Poster presented at the 6th International Conference on the Tear Film and Ocular Surface: Basic Science and Clinical Relevance. Florence, Italy. 24 Sept 2010.

Therapeutic management



Therapeutic management

- Correct eyelid abnormalities
- Normalize lid margin
- Correct surface irregularities

- Stabilize tear film
- Control MGD
 - Lid hygiene
- Reduce inflammation

Management of Dry Eye



- In aqueous tear deficiency
 - Use of **preservative-free artificial tears**
 - Use of **punctal plugs** can prevent tear drainage and prolong the effects of tear substitutes.

Huang B et al. Am. J. Ophthalmol. 137(1), 52–61 (2004).
 Khalil MB et al. J. Refract. Surg. 23(5), 467–471 (2007).
 Yung YH et al. Jpn J. Ophthalmol. 56(3), 208–213 (2012).

Management of Dry Eye Punctal plugs



- Punctal occlusion does not reduce inflammatory mediators
- Punctal occlusion may exacerbate symptoms of blepharitis, so this must be treated beforehand
- The Delphi treatment guidelines for ocular surface disorders recommends that ***inflammatory conditions be treated before punctal occlusion***

[1] Pflugfelder SC. Antiinflammatory therapy for dry eye. Am J Ophthalmol. 2004 Feb;137(2):337-42.
 [2] Tong L, Beuerman R, Simonyi S, Hollander DA, Stern ME. Effects of Punctal Occlusion on Clinical Signs and Symptoms and Tear Cytokine Levels in Patients With Dry Eye. Ocul Surf. 2016 Jan 13.
 [3] ImBehrens A, Doyle JJ, Stern L, et al. The Dysfunctional Tear Syndrome Study Group. Dysfunctional tear syndrome: a Delphi approach to treatment recommendations. Cornea. 2006;25:900-907.

Management of Dry Eye



- In lipid layer deficiency (MGD)
 - use of lid hygiene,
 - warm compress and lid warming
 - nutritional supplement
 - topical azithromycin and
 - oral doxycycline
 - lubricants with lipids

Shtein RM. Expert Rev. Ophthalmol. 6(5), 575–582 (2011).
Toda I. Cornea. Suppl 1:570-6 (2008)

Management of Dry Eye

Control ocular surface inflammation

- **The choice of steroids depends on the severity of inflammation**
Weak topical steroids (fluorometholone, or prednisolone 0.5% PF) can be used on an 'as required' basis or as short tapering courses
In severe inflammation (e.g. acute vernal keratoconjunctivitis), more potent topical steroids (e.g. dexamethasone 0.1%, or Prednisolone 1%) are required

Donnenfeld E, Pflugfelder SC. Surv. Ophthalmol. 54(3), 321–338 (2009).
Salib GM et al. J. Cataract Refract. Surg. 32(5), 772–778 (2006).
Hessert D et al. J. Cataract Refract. Surg. 39(4), 539–547 (2013).
Ursea R et al. J. Refract. Surg. 24(5), 473–476 (2008).
Sall K et al. Ophthalmology 107(4), 631–639 (2000).

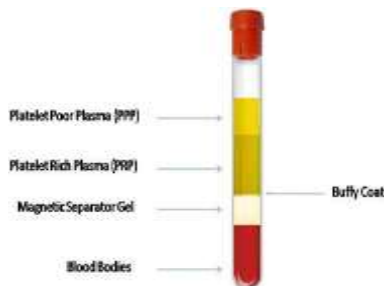
Management of Dry Eye

Control ocular surface inflammation

- **Topical ciclosporin A (CsA)** (various preparations) has been shown to be effective in several ocular surface disorders without the adverse effects of steroids. However, ciclosporin is often poorly tolerated during disease exacerbations and its full efficacy is only achieved several weeks from the initial dose
- Ciclosporin has been shown to be better tolerated if introduced following a few weeks of treatment with topical steroids

Donnenfeld E, Pflugfelder SC. *Surv. Ophthalmol.* 54(3), 321–338 (2009).
 Salib GM et al. *J. Cataract Refract. Surg.* 32(5), 772–778 (2006).
 Hesse D et al. *J. Cataract Refract. Surg.* 39(4), 539–547 (2013).
 Ursea R et al. *J. Refract. Surg.* 24(5), 473–476 (2008).
 Sall K et al. *Ophthalmology* 107(4), 631–639 (2000).

Management of Dry Eye



- Eye platelet rich plasma (E-PRP) has been shown to reduce punctate epithelial erosion, increase tear film stability and improve best corrected visual acuity following surgery

Javaloy J et al. *J. Refract. Surg.* 29(3), 213–219 (2013).
 Alio JL et al. *J. Refract. Surg.* 23(6), 617–619 (2007).
 Alio JL et al. *Curr. Pharm. Biotechnol.* 13(7), 1257–1265 (2012).

PERFECTION
is lots of little things done well

– Fernand Point –

A Healthy Ocular Surface means
that a lot of *“little things”* go well



**THANK YOU
FOR YOUR
ATTENTION**

