TEAR OSMOLARITY : A CLINICAL TOOL FOR THE DIAGNOSIS AND MANAGEMENT OF OSD

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DISCLOSURE

Historical affiliations

- I-MED pharma
- Alcon
- Alden Optical

Eye Am
SOINS OCULAIRES

Co-owner and practicing optometrist with special interest in Dry Eye management and specialty contact lenses.

Brio

Briller par l'excellence

Co-owner and responsible of initial and ongoing training for staff and OD's in Dry Eye management in our partner clinics.

LEARNING OBJECTIVES

- Reviewing the importance of Dry Eye disease in clinical care
- Reviewing the basics of tear film osmolarity
- Optimizing ocular surface disease diagnosis/management using tear osmolarity
- Learning clinical applications of tear osmolarity

DRY EYE DISEASE OVERVIEW

- Prevalence is somewhere between **10-25%** in general population.
- One of the **leading cause** of in-office consultations with ECP.
- This number is expected to **increase** in the years to come.
- DED is a public health issue with a **significant cost** both financially and to the quality of life of those affected.

RISK FACTORS FOR DED

- Age
- Female gender
- Systemic/topical Rx
- Hx eye/lid surgery or abnormality
- Smoking
- Systemic disease
- Environnemental
- Contact lens wear
- Diet (Low essential fatty acids)

SPECIFIC PATIENT POPULATIONS

Higher prevalence

- Asian descent population
- Older patients
- Glaucoma patients
- Contact lens wearers

DEWS DEFINITION

"Dry Eye is a multifactorial disease of the tears and ocular surface that results in symptoms of discomfort, visual disturbance, and tear film instability with potential damage to the ocular surface. It is accompanied by increased **osmolarity** of the tear film and **inflammation** of the ocular surface."

Two main types of DED; each with multiple subsets

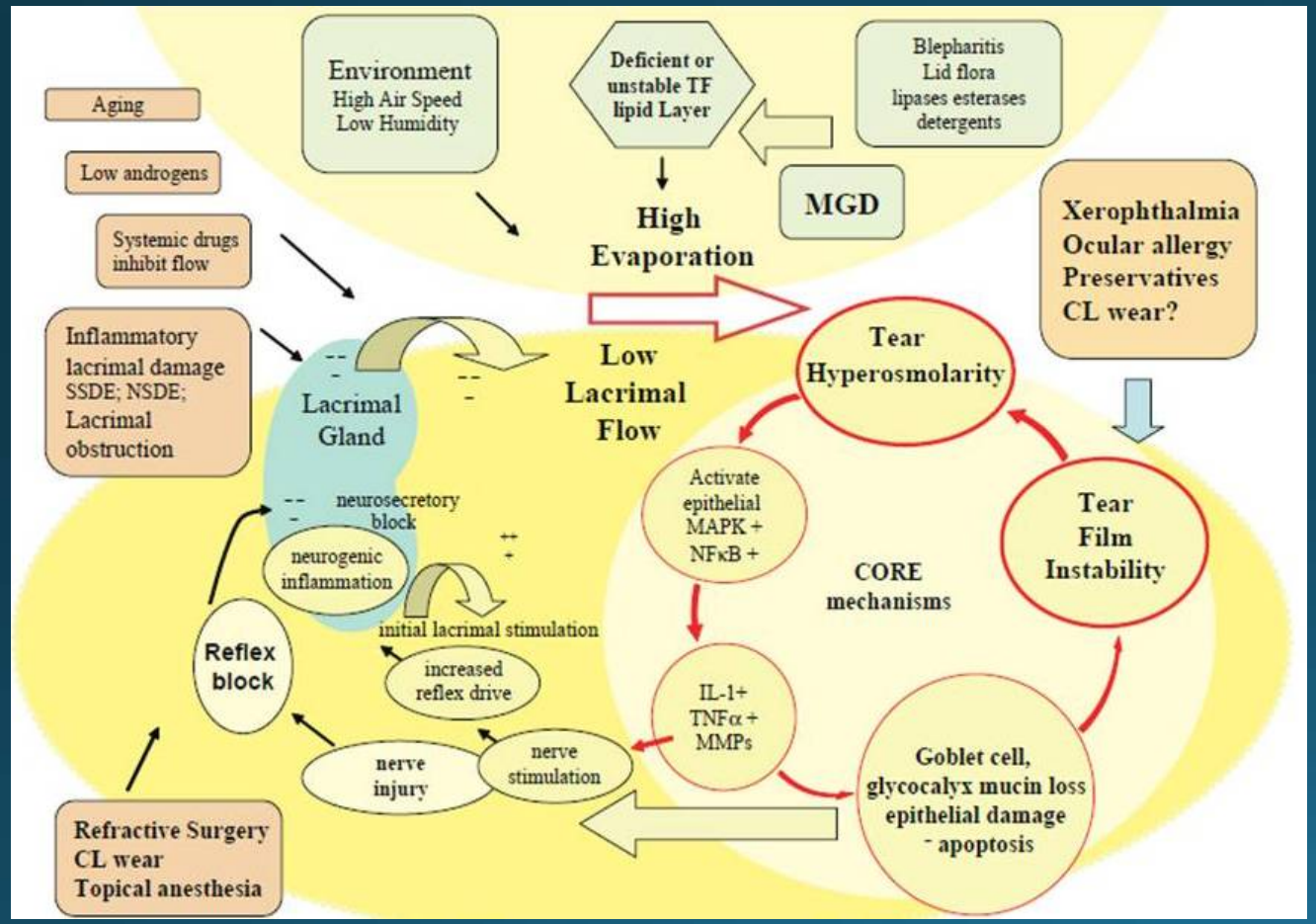
- **Aqueous deficient** dry eye
- **Evaporative** dry eye

Ref: Report of the International Dry Eye Workshop, Ocular surface April, 2007 5(2) 119

DEWS II DEFINITION

"Dry Eye is a multifactorial disease of the ocular surface characterized by a loss of homeostasis of the film, and accompanied by ocular symptoms, in which tear film instability and hyperosmolarity, ocular surface inflammation and damage, and neurosensory abnormalitites play etiological roles".

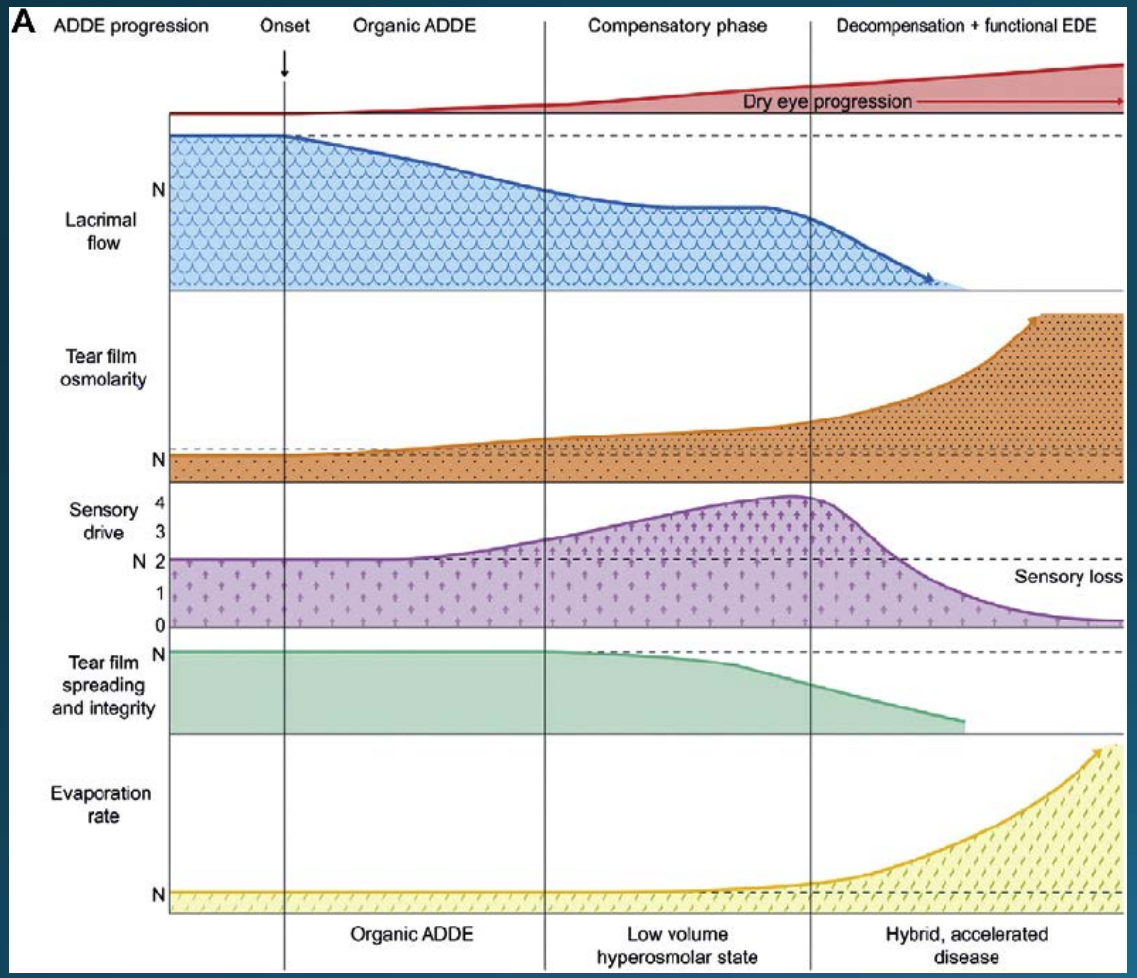
MECHANISMS OF DED

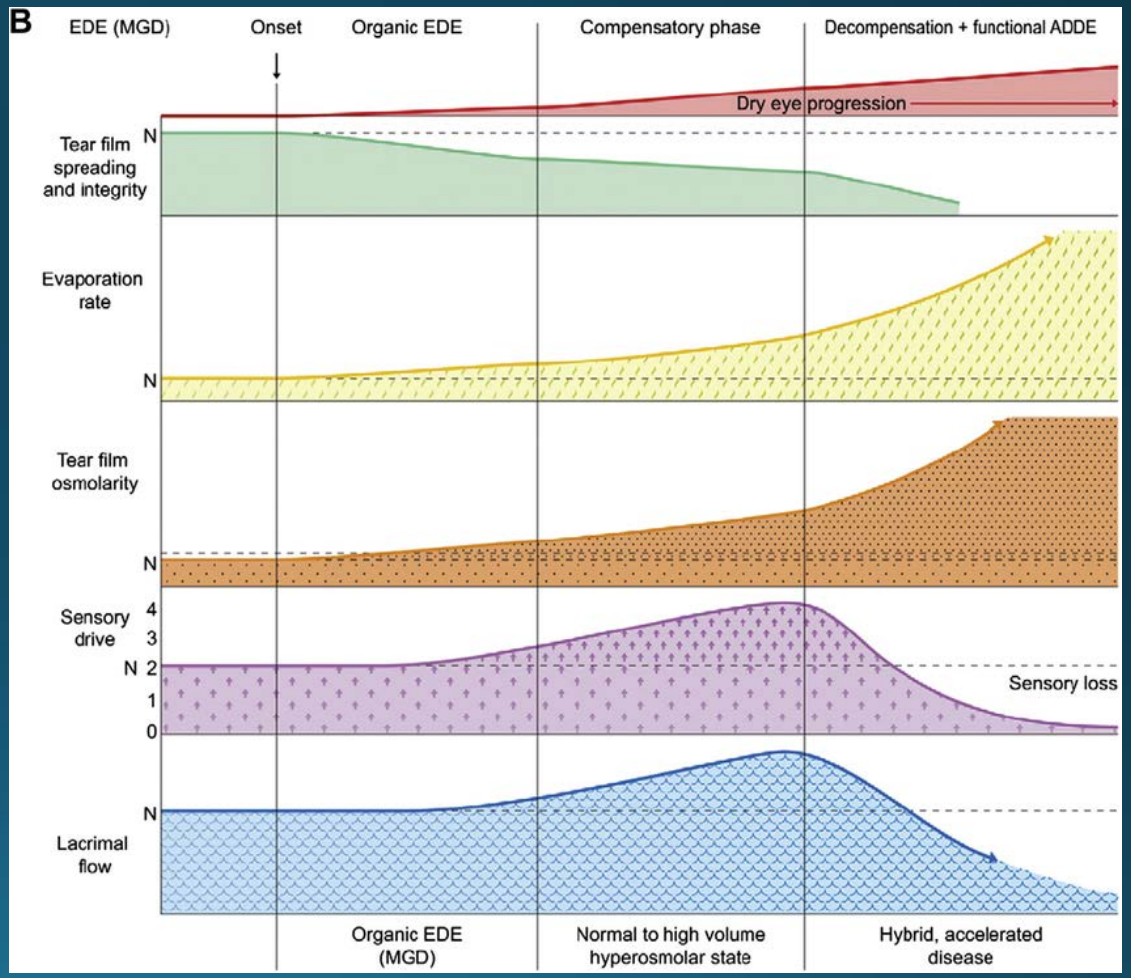


Tear **osmolarity** is with tear **instability** among the core mechanisms behind DED, therefore the necessity to measure it.

Ref: Lemp &Foulks. Figure 2. Mechanisms of dry eye, April 2008.

NATURAL EVOLUTION OF ADDE/EDE





Ref : Predicted phenotypes of dry eye : proposed consequences of its natural history. (Ocular surface, 2009:7(2) p. 78-92)

THE CHALLENGE OF DED SCREENING

- Lack of correlation between **signs** and **symptoms**.
- There is **no single test** that's 100% reliable to distinguish dry eye patients from normal.
- **Early detection** is key in stopping progression but also harder because of lack of clinical signs.

IMPORTANCE OF EARLY INTERVENTION IN CHRONIC AND EVOLUTIVE CONDITIONS

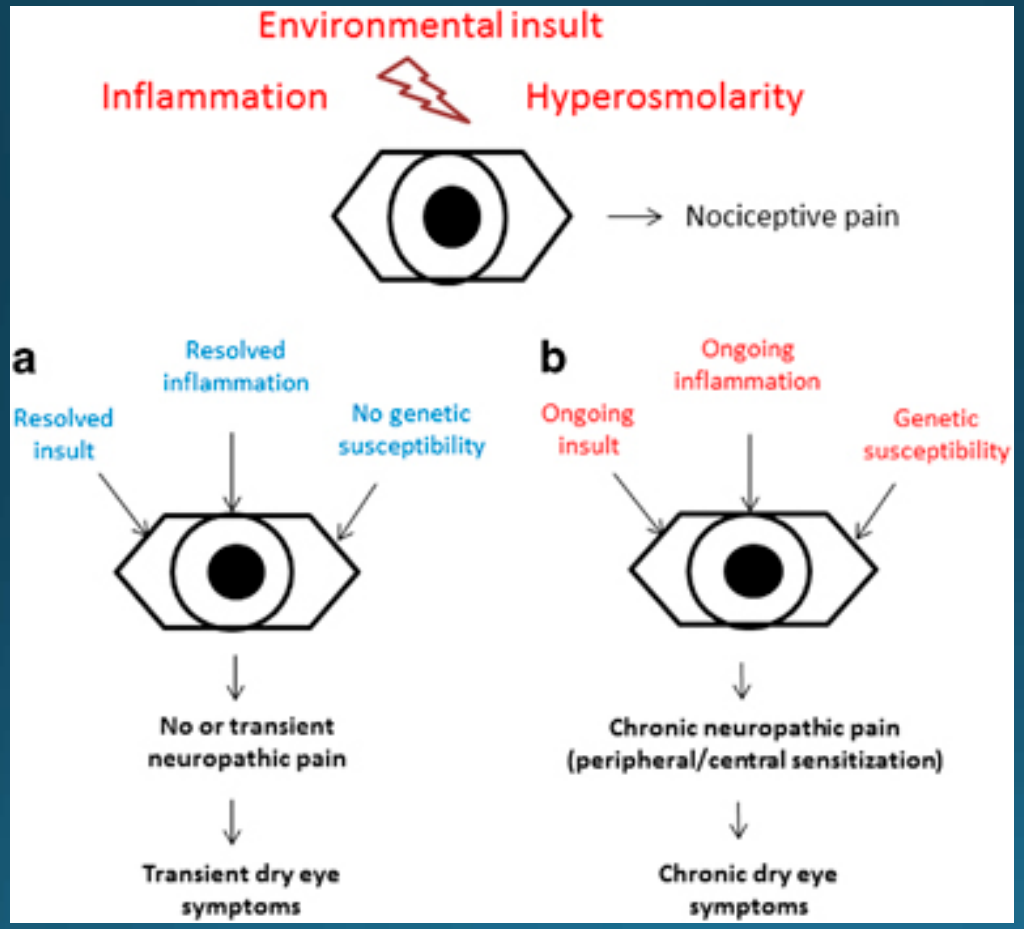
- The most obvious indicators :

  Symptoms and staining $\neq$ Early indicators of DED

- We have more tools than ever to make early diagnosis of DED.

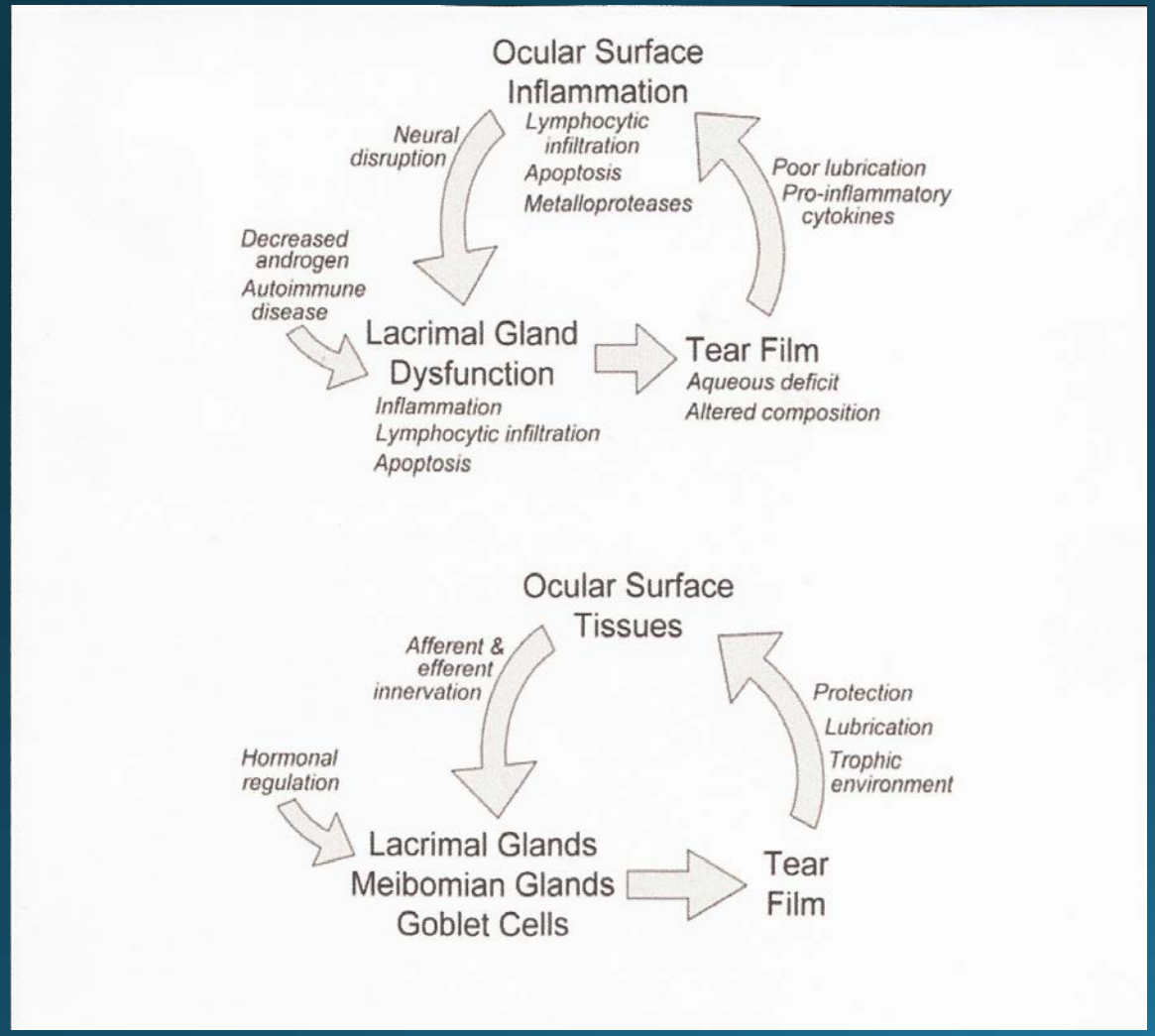
- We would not wait until visual field defect is measurable to treat glaucoma.

EXAMPLE OF EARLY INTERVENTION PREVENTING LONG-TERM COMPLICATIONS



Ref : Figure 4. Galor A, Levitt RC, Felix ER, Martin ER, Sarantopoulos CD. Neuropathic ocular pain: an important yet underevaluated feature of dry eye. Eye (Lond); March 2015; 29 (3), pp. 301-312

LACRIMAL FUNCTIONAL UNIT (LFU)



LFU is the integrated neural network that connects the ocular surface (cornea, conjunctiva, main and accessory lacrimal glands) that has the function of maintaining **homeostasis** of the ocular surface as a whole.

Ref: Pflugfelder Sc, Stern Me. Dry Eye:Inflammation of the Lacrimal Function Unit.Uveitis and Immunological Disorders. Part of Essentials of ophtallmologyp.11-24.

Imbalance of the LFU leads to a **hyperosmolar**, and **pro-inflammatory** tear film, inducing the DED cycle and loss of **homeostasis.**

Afferent system interruption

- Contact lens wear
- LASIK
- Herpetic keratopathy
- Diabetes

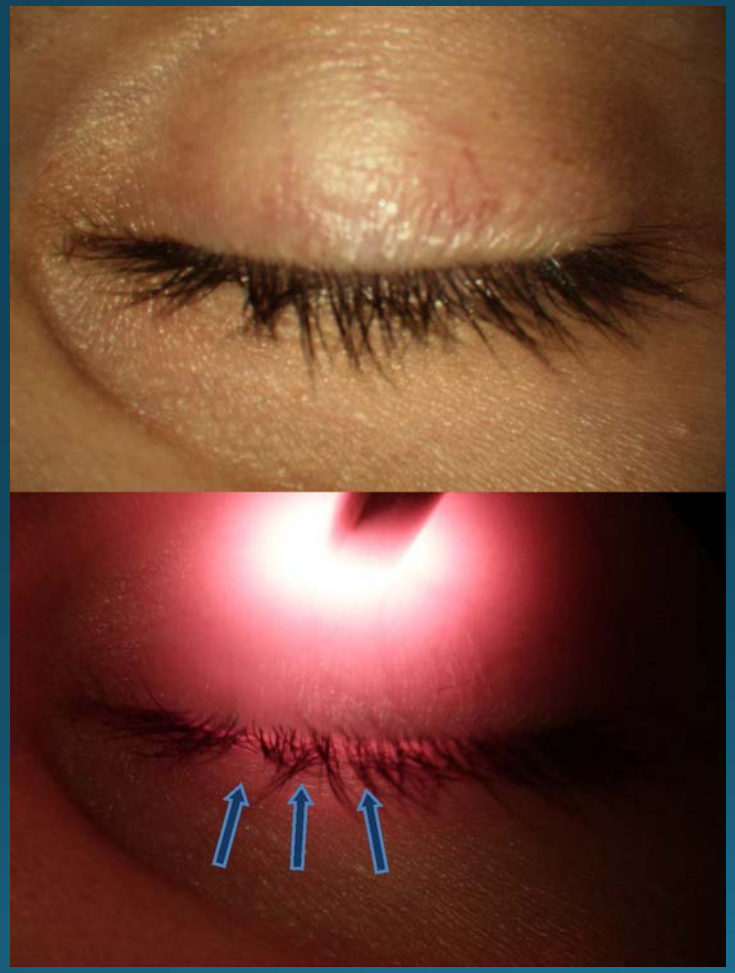
Efferent system interruption

- Secondary to systemic drugs
- Associated with age

EXAMPLE OF DED/OSD ASSESSMENT

1. Case history/Dry Eye questionnaire
2. External examination (Facial asymetry, lid abnormalities, etc,…)
3. Tear film interferometry/Blink analysis
4. Meibography
5. Osmolarity
6. Phenol red thread test/ Shirmer I
7. RPS/Inflammadry(MMP-9)
8. SLEX lamp/white light/lid margin
9. Korb/Blackie light test
10. TBUT
11. Ocular surface staining; cornea and conjonctiva
12. Meibomiam gland evaluation /expression

KORB/BLAKIE LIGHT TEST

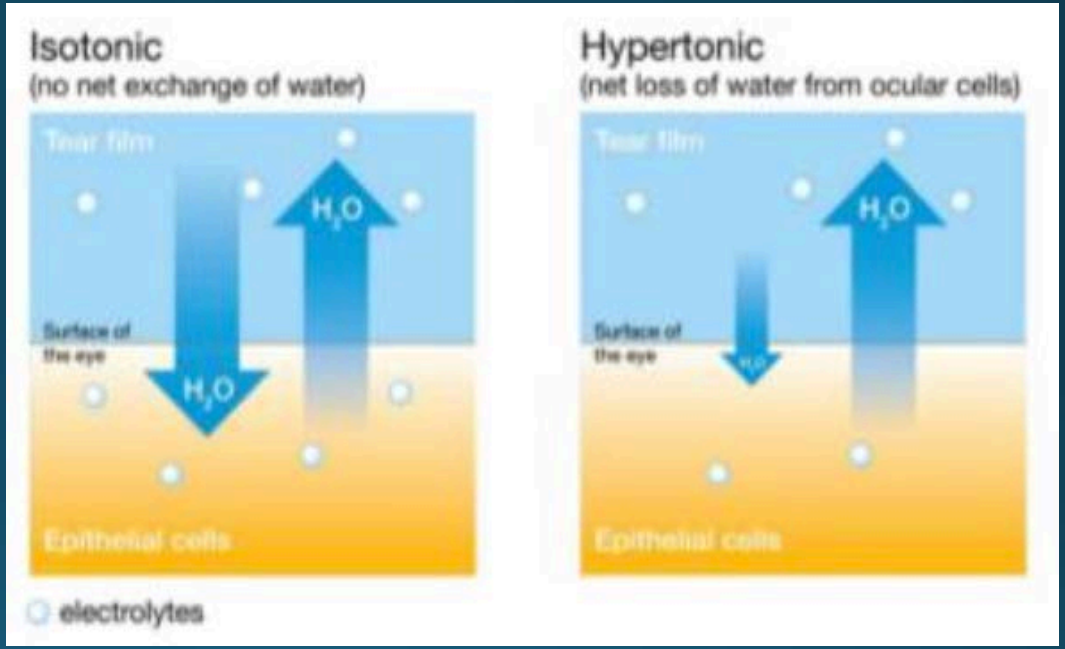


WHY SO MANY TESTS TO PERFORM IN DED ASSESSMENT?

- No single test available with definitive ability to diagnose dry eye.
- Lack of correlation between signs and symptoms.
- Many potential causes to DED

CONCEPT OF OSMOLARITY

Osmolarity is the measure of solute concentration defined as the number of osmoles(OSM) of solute per litre(L) of solution (osmol/L or OSM/L).

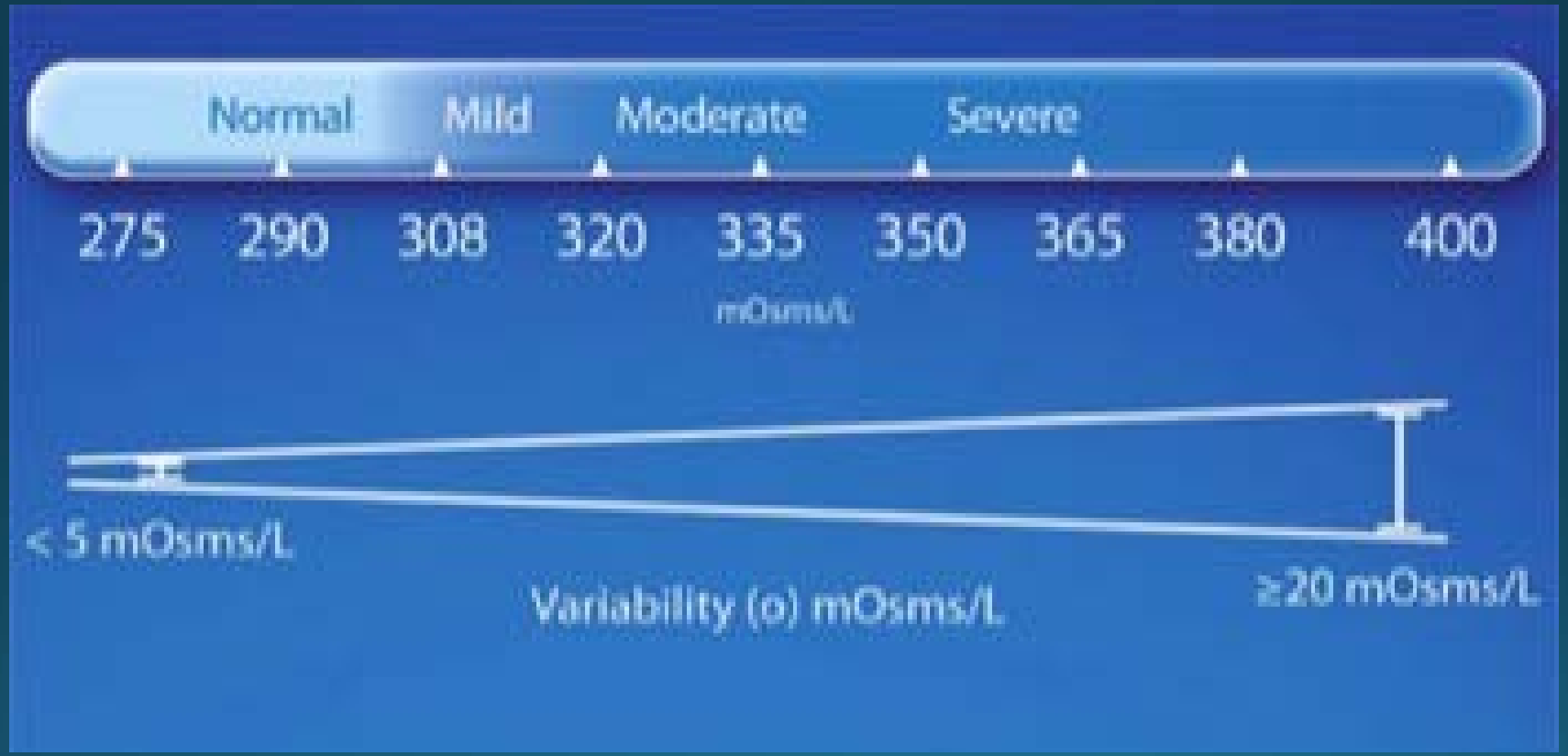


Ref : Report of the Internation Dry Eye Workshop, Ocul Surf April 2007; 5(2) p. 119 6. Liu H. et al. A link between tear instability and hyperosmolarity in Dry Eye. Invest Ophtalmol. Vie sol. 2009 Aug-50(B) 3671-9 Epub 2009 May 25.

METHODS OF OSMOLARITY TESTING

- Freezing point depression; sample 0,2 microl
- Vapour pressor; sample 5 microl
- Electrical impedance; sample 50 nanol
  - Correlation between osmolarity and conductivity of a solution
  - Clinically available testing devices use this principle for ease of use and smaller sample size

TEAR FILM OSMOLARITY SEVERITY/VARIABILITY SCALE



TEAR LAB

I-PEN®

- Stand alone unit
- Single use sensors
- In vivo measurement
- No discomfort to patients
- Quick procedure <5 sec.

i-med PHARMA INC.

STATISTICAL DEFINITIONS

- **Sensitivity** (also called the true positive rate) : Measures the proportion of positives that are correctly identified as such(e.g., the percentage of sick people who are correctly identified as having the condition).

- **Specificity** (also called the true negative rate) : Measures the proportion of negatives that are correctly identified as such (e.g., the percentage of healthy people who are correctly identified as not having the condition).

- **Positive predictive value** (PPV) : Is the probability that a person with a with a positive test result has, or will get, the disease.

TEAR OSMOLARITY IN THE DIAGNOSIS AND MANAGEMENT OF DED (LEMP ET AL 2011)

Most **sensitive** threshold between normal and mild or moderate DED

308mOsm/l

Most **specific** threshold

315 mOsm/l

Intereye difference

>8 mOsm/l

At **312 mOsm/l**

73% sensitivity

92% specificity

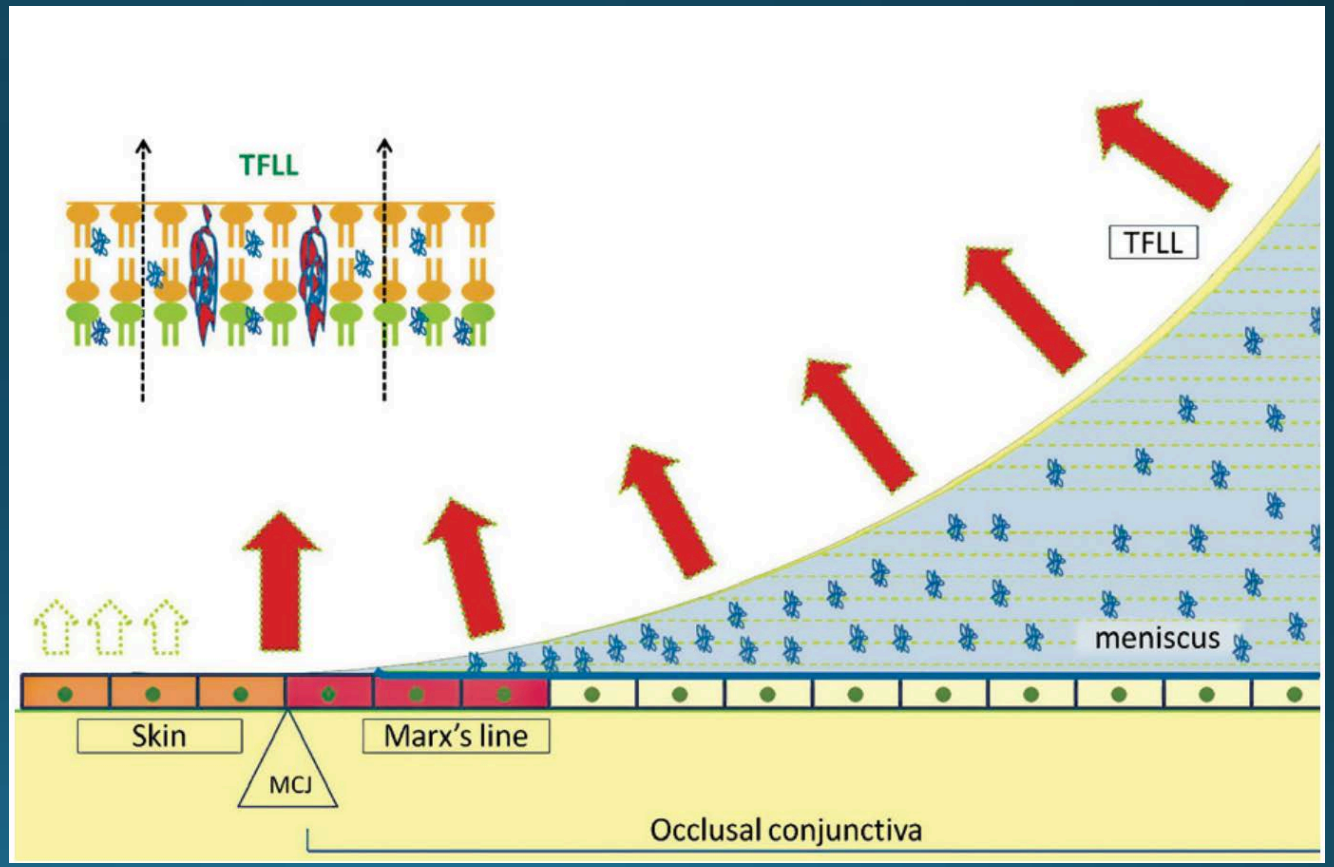
Conclusion :

"Tear osmolarity is the **best single metric** both to diagnose and classify DED. **Intereye variability** is a characteristic of dry eye not seen in normal subjects."

Ref : Tear osmolarity in the diagnosis and management of DED, Lemp, et al, Am J. Ophtalmol. 2011 May; 151(5): 792-798.

OSMOLARITY WITHIN THE TEAR MENISCUS

Osmolarity at the inferior apex the meniscus is hypothesized to be responsible for the Marx's Line formation.



Ref :Solute gradient in tear meniscus. I. Marx's Line hypothesis, Bron et Al, The ocular surface, April 2011, vol. 9, n.2

- Hyperosmolarity and chronic exposure may also lead to meibomian gland damage.
- Clinically visible with anterior migration of Marx's Line.

Masquerading conditions – symptomatic patients with normal osmolarity

- Conjunctivochalasis
- RCE
- Blepharitis
- EBMD
- Mucus fishing syndrome
- Floppy eyelid syndrome
- GPC/Allergy
- Salzmann nodular degeneration
- Binocular anomalies

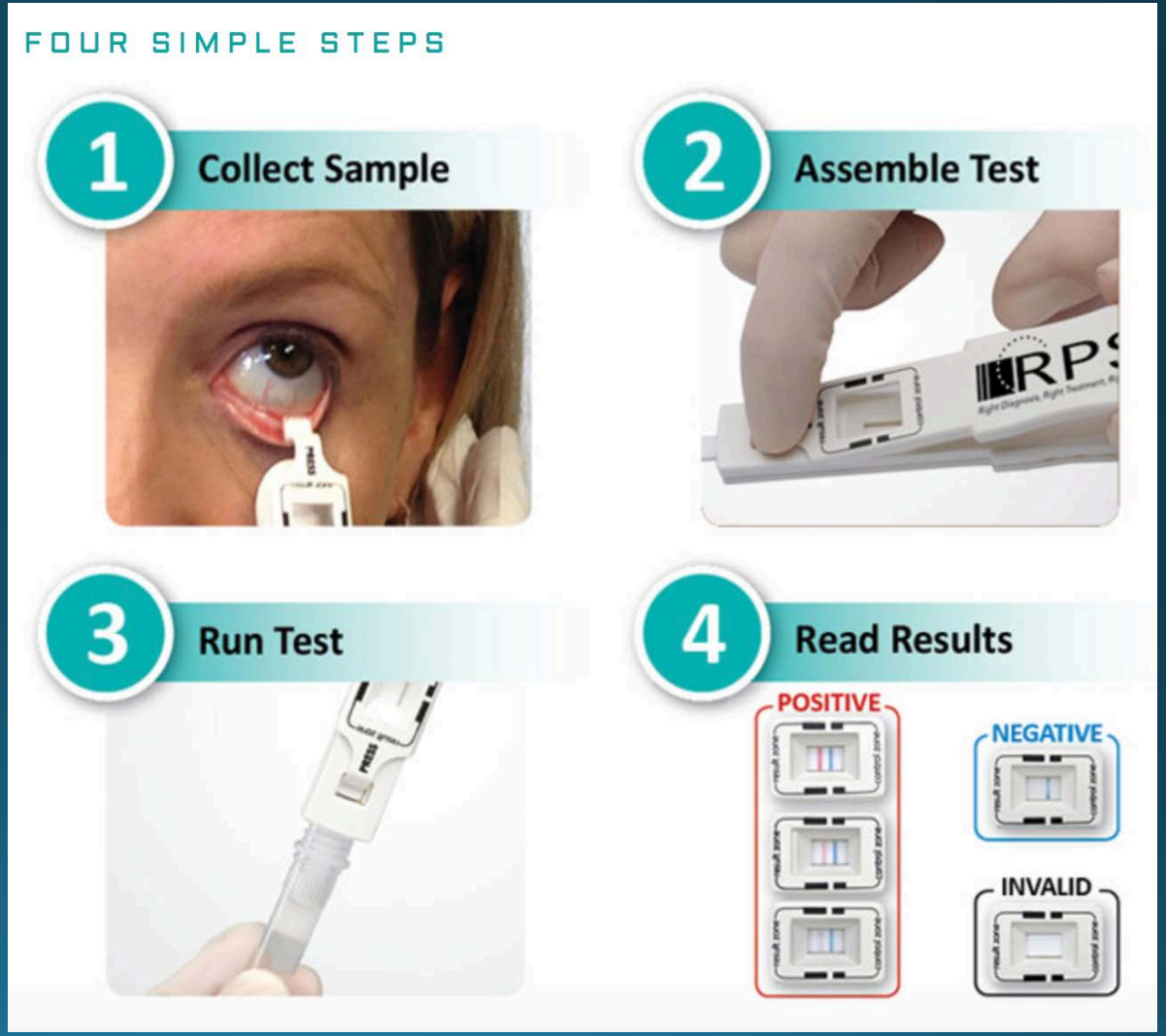
INFLAMMATORY BIOMARKERS

- Chronic ocular surface inflammation, that can be caused by a hyperosmolar state, is known to increase the level of tear film inflammatory markers.

- Among them, MMP-9(Matrix metalloproteinase-9) is clinically measurable and an objective indicator of DED and other conditions associated with significant ocular surface damage.

RPS/INFLAMMADRY

- Clinically available test for in-vitro detection of MMP-9 in the tear film
- MMP-9 / non-specific marker of DED
- Gives a positive/negative result (positive if MMP-9 ≥40 ng/ml)



MAHARAJ OCULAR SURFACE CLASSIFICATION MODEL

	Cat. 1	Cat. 2	Cat. 3	Cat. 4
Tear osmolarity	Normal	High	High	Normal
MMP-9	Negative	Negative	Positive	Positive
Diagnostic status	Non-DED	Early DED or on current MMP-9 Tx treat other aspects of tear dysfunction (MGD)	Moderate to severe DED	Post-operative, Cch, EBMD, other etiology, may not be tear dysfunction : Ex : Allergy

The use of a "tear panel" with osmolarity and MMP-9 is of clinical value in differential diagnosis of OSD and helps better target the therapy/management.

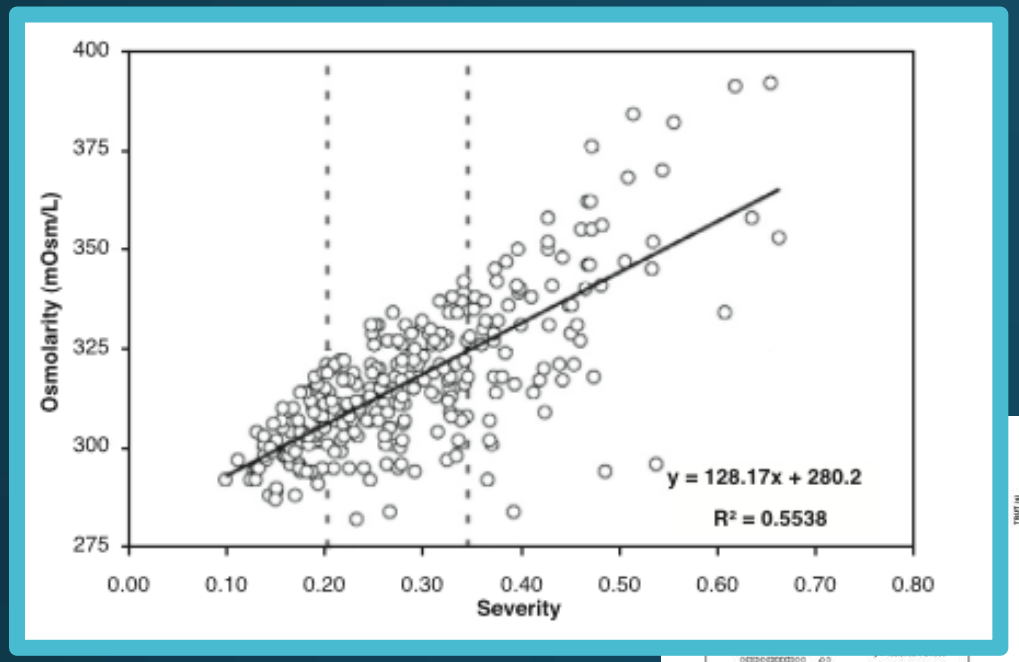
DED/OSD SCREENING

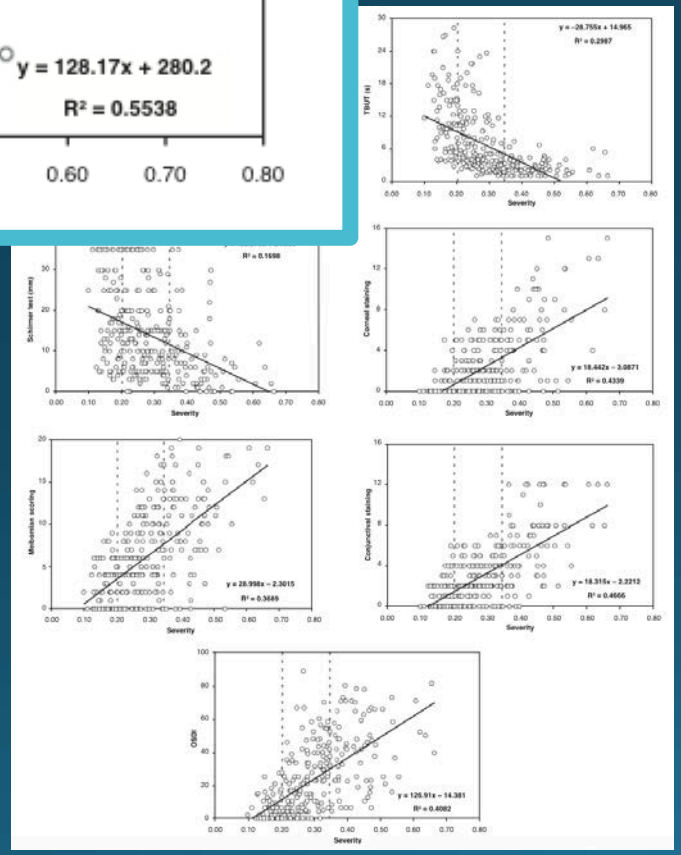
Because of its ease of use and strong correlation with the presence of DED, tear film osmolarity can easily be performed routinely in combination with a dry eye questionnaire to obtain a very good screening of DED/OSD patients.

DED screening is becoming standard of care due to the high prevalence of this condition and the known complications of its later stages.

EX:

- Non-resolving surface damage
- Neuropathic eye pain
- Visual compromise





We need to remember that not only is tear film osmolarity a more reliable indicator of DED, it also has a stronger correlation than any other test for it's mild or moderate stage.

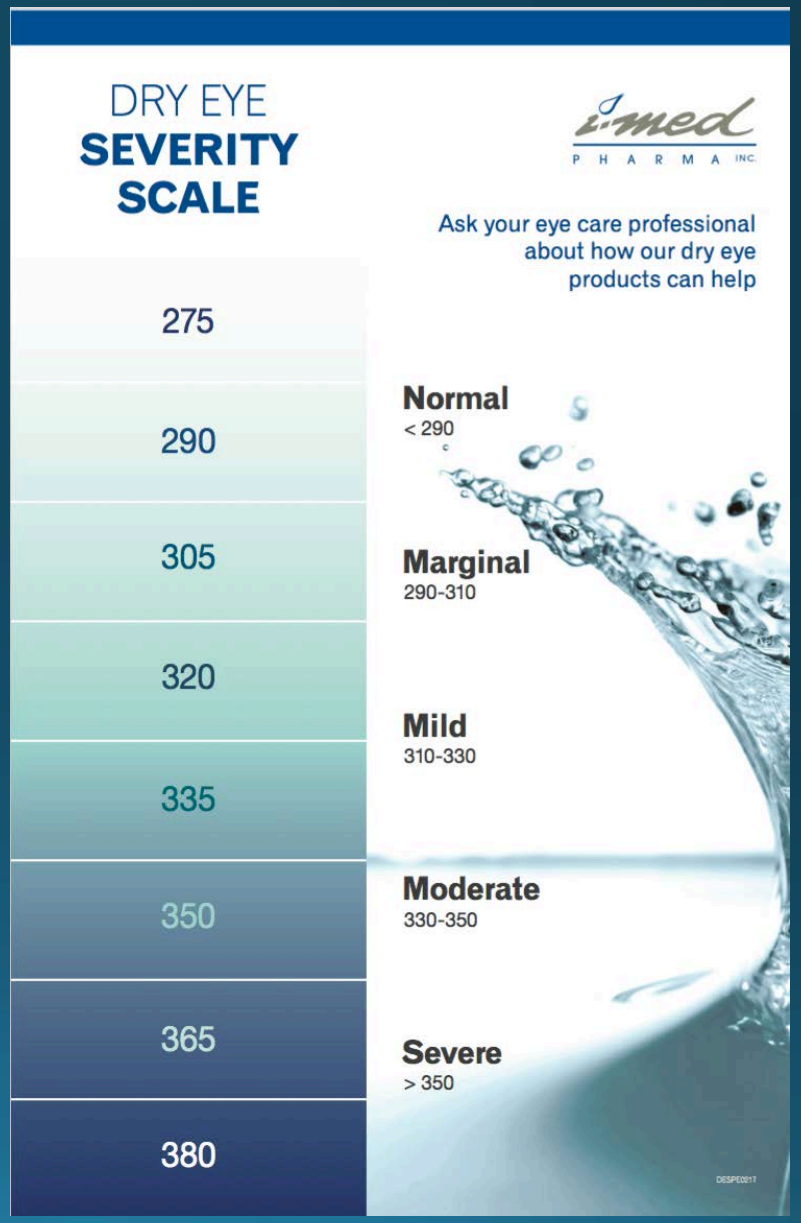
Ref : Ocean group proceeding, The ocular surface, October 2013, vol. 11, n.4.

Osmolarity has another interesting attribute, it also predicts the severity of DED with a very high correlation.

2 major implications :

- It helps us initiate appropriate therapy in regard of the severity of the presentation.

- Guides us in the long term management of the condition; similar as blood sugar levels for patients with diabetes.



OSMOPROTECTION

- From the beginning, avoiding **BAK** which is known to be detrimental to the ocular surface is a sound choice.
- Drops containing **hyaluronic acid, L-carnitine**, **erythritol** and **betaine** are known to have a positive impact on tear film osmolarity.
- For patients using eye drops more than 3-4 times a day or compromised ocular surface, **preservative free** lubricants are usually recommended.

DED AND CONTACT LENS CARE

- Even with today's newest materials and care solutions the drop out rate in contact lens wearers remains high, the main cause being discomfort.

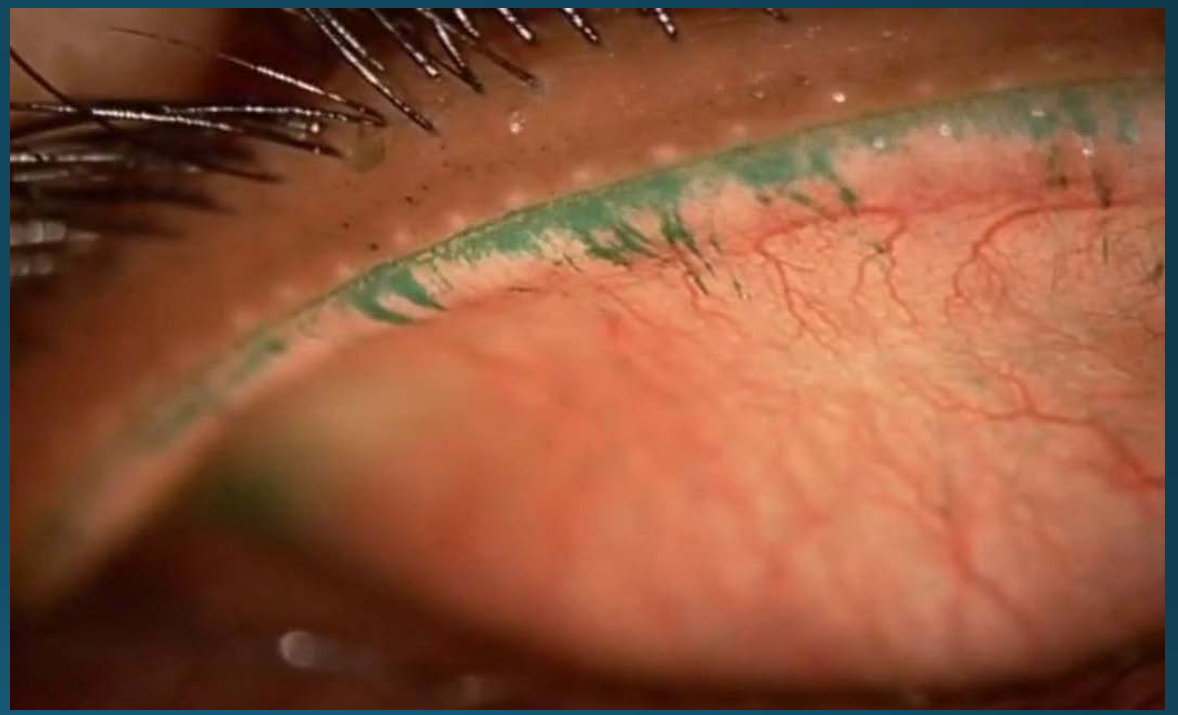
- "CLIDE" (contact lens induced dry eye) is very common (≈50%) among wearers, we can prevent it instead of managing it by paying sufficient attention to early signs, even in "comfortable wearers" (namely tear osmolarity).

- Careful screening of DED in **potential** contact lens wearers is of foremost importance to avoid discomfort, complications and ultimately contact lens drop-out.

- Surface hypersomolarity has been linked to ↓ **Dk** in some contact lens materials, another good reason to maintain a healthy surface in contact lens wearers.

- Mechanical forces at play in blinking will usually cause no shear stress on the involved surfaces in non-DED patients and well fitted contact lens wearers.

- This is not the case in DED patients where the decreased quantity and quality of the tear film will induce discomfort but also damage to sensitive areas mainly the lid wiper.



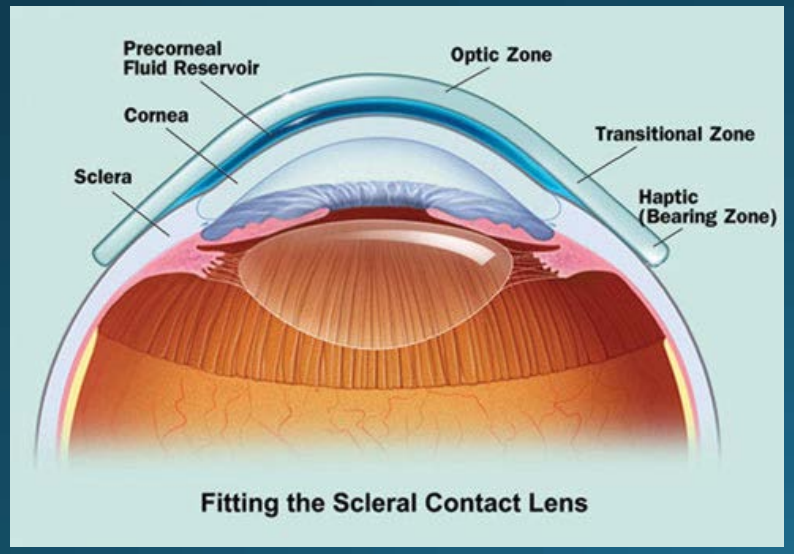
Modifiable parameters

- Increase quality and stability of the tear film prior to fitting.

- Decrease frictional forces by optimizing the contact lens parameters

  - ↑**Wettability** (material, solutions, replacement schedule)
  - ↓**Modulus** Making it similar to the ocular surface
    (Modulus is linked to LWE/LIPCOF)
  - Use thin and smooth **edge designs**

- Because of the improved fitting techniques and numerous parameters, scleral lenses are a very efficient tool in DED patients, especially those with persistent epithelial compromise.



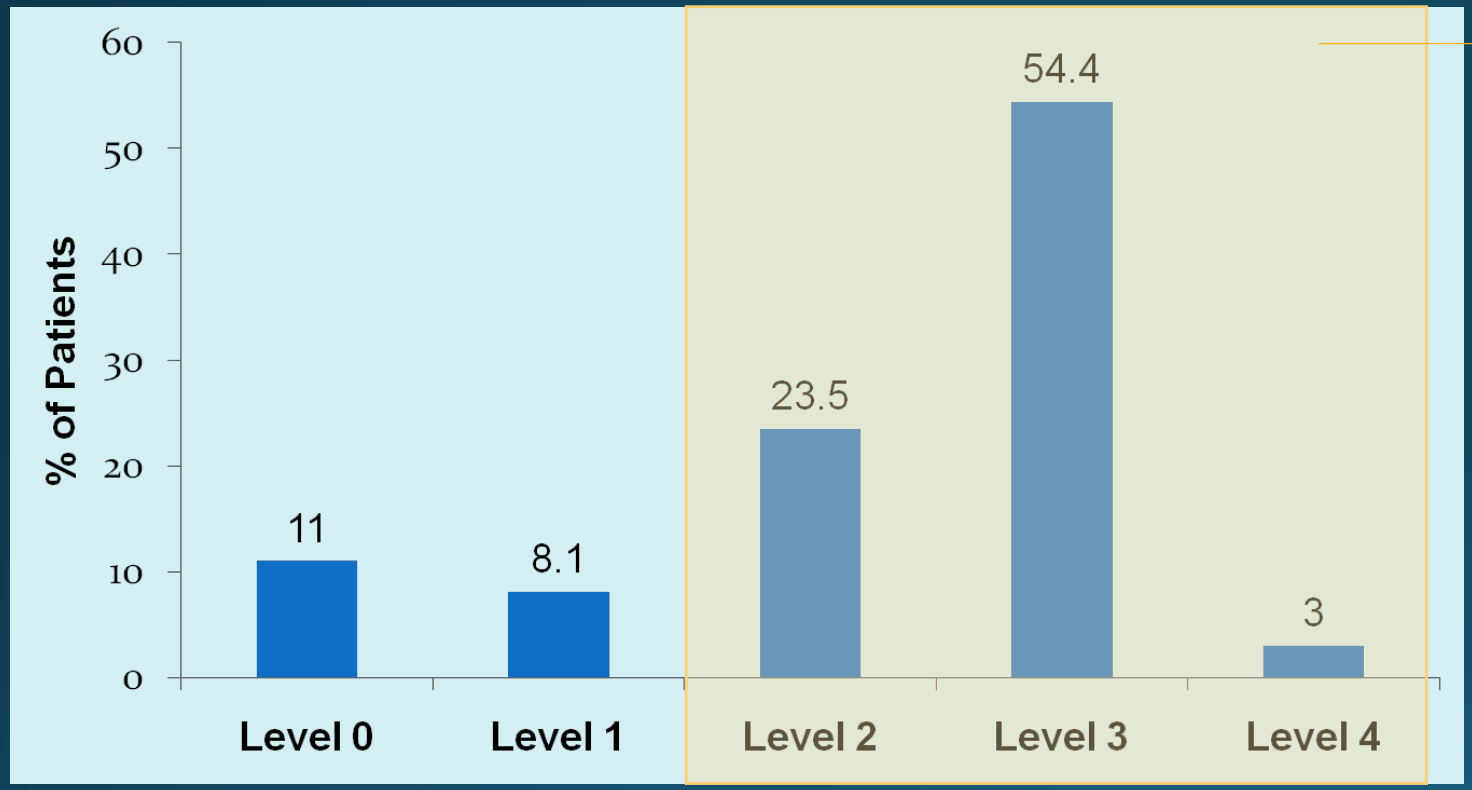
Fitting the Scleral Contact Lens

- For DED patients, a combination of HA and non-preserved saline can be useful.

DED IN PERI-SURGICAL CARE

- Avoid evitable worsening of the condition.
- Obtain reliable pre-op data; mainly keratometry.
- Optimize visual function through a healthy ocular surface.
- Create optimal patient experience in surgical comanagement; create better relation with surgeons.

PHACO STUDY

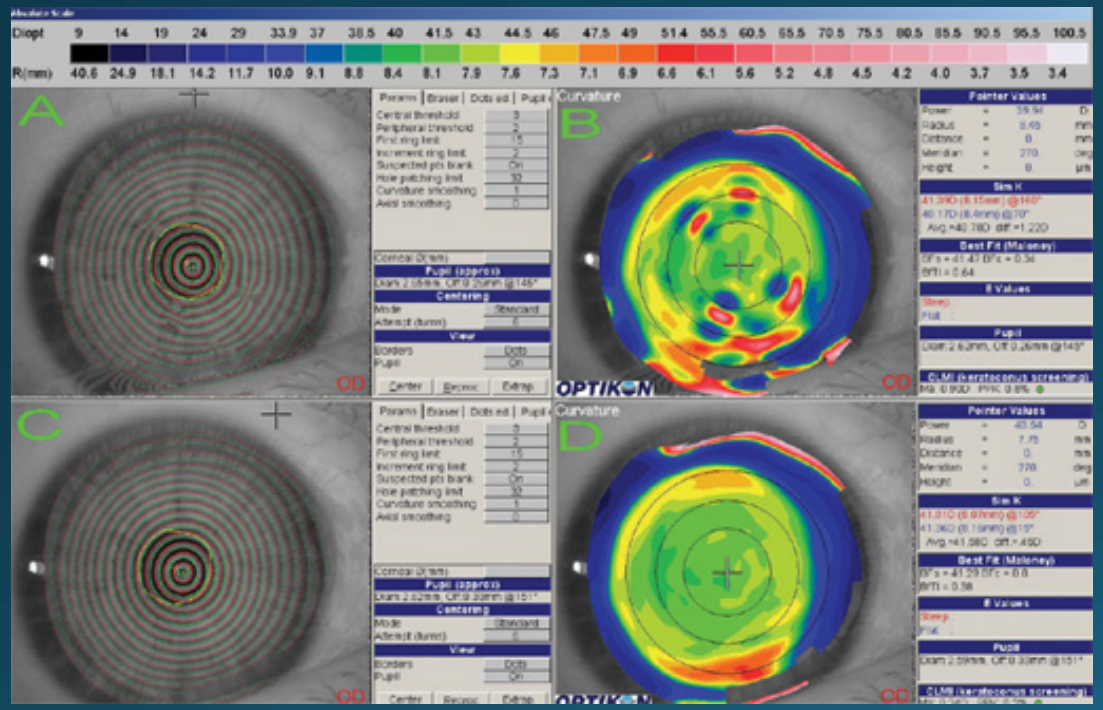


81% have moderate to severe DED

Only 22% had a Dx of DED prior to consult

Ref :Cataract and Dry Eye : Prospective Health Assessment of Cataract Patients Ocular Surface Study, *W. B. Trattler; C. D. Reilly; D. F. Goldberg; P. A. Majmudar; J. A. Vukich; M. Packer; E. D. Donnenfeld, eposter, ASCRS,2011*

Tear osmolarity on repeatability of keratometry



"Measurement of tear osmolarity at the time of cataract surgery planning can effectively identify patients with a higher likelihood of high unexpected refractive error resulting from inaccurate keratometry".

Ref : Effect of tear film osmolarity on repeatability of keratometry for cataract surgery planning, J cataract refract surg; 2015 August, 41(8), pp.1672-1677

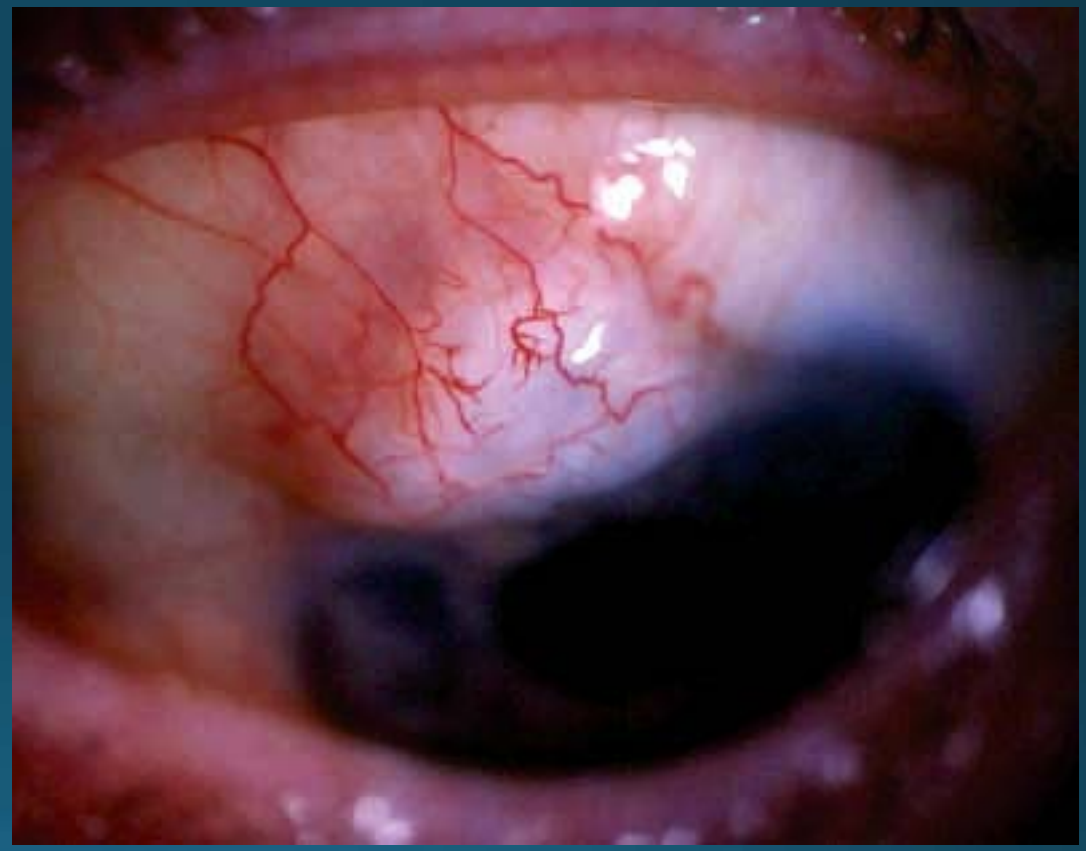
DED IN GLAUCOMA PATIENTS

- Prevalence of DED in glaucoma patients is significantly higher than in non-glaucoma patients.
- Prevalence is higher in patients on preserved medications and on polytherapy.
- Comorbidity, age and pre-existing OSD also explain higher prevalence of DED in these patients.
- Preservatives (mainly BAK) are known to be detrimental to :
  - Corneal epithelium (affecting tight junctions)
  - Conjunctiva (causing loss of goblet cells)

- Because of the **chronic nature** of both glaucoma and DED, screening glaucoma patients is important to avoid worsening.
- We can also play a proactive role in that sense by optimally screen and pre-treat DED/OSD in glaucoma suspects **before** they are put on long term topical medications.
- Tear film **osmolarity** shows a very good correlation with DED in glaucoma patients.

- Adressing OSD/DED in glaucoma patients not only minimizes discomfort but also tends to help with long term compliance to therapy.

- A number of studies also link OSD to an increased risk of filtering surgery failure.

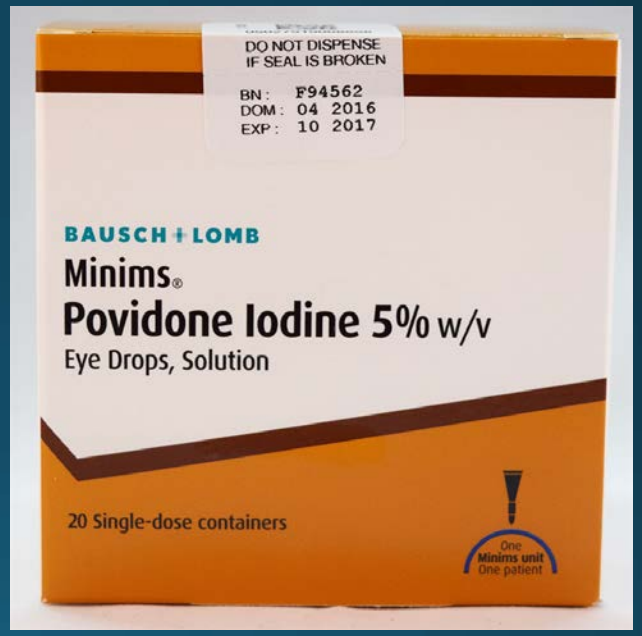


"We speculate that POAG patients needing long-term treatment with anti-hypertensive eye drops are at risk of developing DED(or exacerbation a latent DED). The significant role of aging in both DED and POAG may increase the probability of POAG and DED comorbidity. Therefore, we strongly recommend that patients with POAG be carefully evaluated for dry eye symptoms prior to starting any topical antiglaucomatous therapy".

Ref : Patients undergoing long-term treatment with anti-hypertensive eye drops respond positively to oral supplementation with antioxydants and essential fatty acids. Clinical intervention in agine 8; June 2013,p. 711-719.

DED IN AMD PATIENTS

Anti-VEGF injections for wet AMD has an impact on the ocular surface through the repeated use of povidone iodine and lid retractors in the injection protocol.



It is comparable to glaucoma in that:

- Older and more susceptible population
- Presence of comorbidities is frequent
- Repeated exposition to a detrimental procedure

Once again, screening and pre-treatment of OSD/DED should be discussed with these patients.

- Optimization of the ocular surface in injected patients once again helps with the discomfort associated with repeated injections; but also can have a positive impact on BCVA.

- The impact of DED on the visual function has been studied for a while but we must not assume that this effect is not significant in wet-AMD patients.

CONCLUSION

- DED/OSD is highly prevalent.
- Those patients are already in your practice.
- Screening and management of DED is an opportunity of growth.
- Tear osmolarity is an indispensable tool for this purpose.

THANK YOU

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