



RECENT ADVANCES IN THE MANAGEMENT AND TREATMENT OF DRY EYE DISEASE

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FINANCIAL DISCLOSURES

Francesco Carones, MD consults for the following companies:

- Alcon Laboratories (not relevant to this presentation)
- CSO (not relevant to this presentation)
- Johnson & Johnson Vision (not relevant to this presentation)
- Slack (not relevant to this presentation)
- Vivior (not relevant to this presentation)
- WaveLight (not relevant to this presentation)



THE IMPORTANCE OF A STABLE TEAR FILM

- A healthy ocular surface is essential for good vision.
- Since 70% of the total refractive power occurs at the tear film surface, it is essential to evaluate the tear film when managing ocular surface disease.
- Unstable tear film deteriorates the retinal image quality resulting in fluctuating vision.
- Visual disturbance is probably the most common DED symptom but patients have difficulty describing it to the doctor.



Dawson D, Watsky M, Geoski D, Edelhauser H. Cornea and Sclera. *Duanes Ophthalmology*. New York, NY: Lippincott Williams & Wilkins; Vol. 2 Chapter 4.



WHY MEASURE TEAR OSMOLARITY?

- Tear osmolarity is a **measure of the solute content** of the tear film.



- Tear osmolarity is an important **biomarker** of ocular surface health.
- Abnormal osmolarity indicates a breakdown of the homeostatic mechanism resulting in an unhealthy tear film, which can potentially damage the ocular surface and cornea.

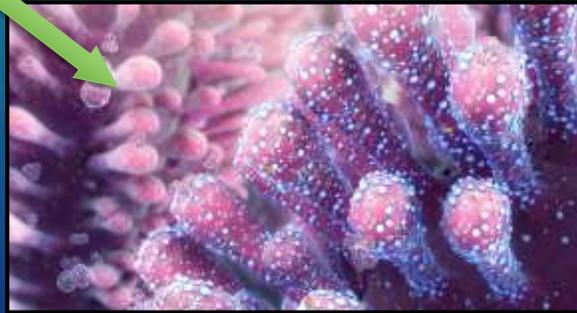
TEAR OSMOLARITY AND OCULAR SURFACE HEALTH



Normal Tear Film – lipid, aqueous and mucous layer.

Decrease in aqueous production or increased evaporation results in abnormal osmolality

The glycocalyx and microvilli help retain water on the corneal surface



TEAR OSMOLARITY AND OCULAR SURFACE HEALTH



LEFT UNDIAGNOSED AND UNTREATED, TEARS WITH ABNORMAL OSMOLARITY BECOME INCREASINGLY CYTOTOXIC TO THE CORNEAL EPITHELIUM

Death to superficial epithelial cells exposes the underlying immature cells to the cytotoxic hyperosmolar tears

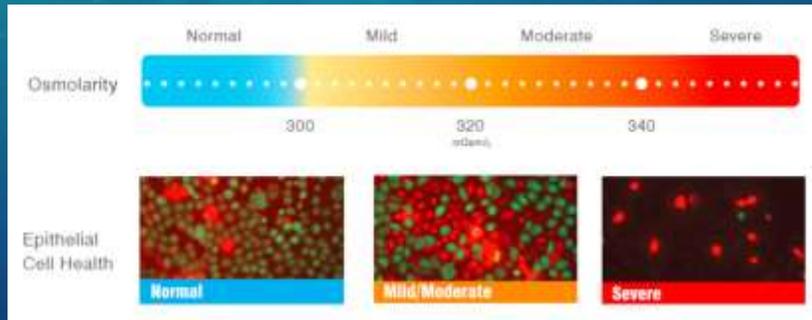


DIAGNOSE: TEST BOTH EYES TO UNCOVER ABNORMAL OSMOLARITY AND DETERMINE SEVERITY

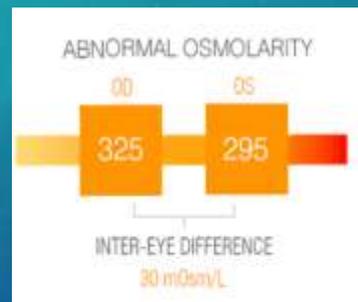
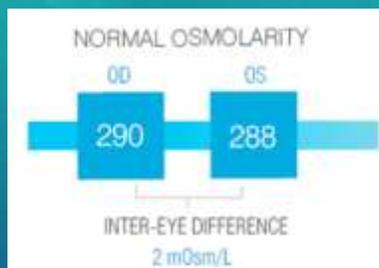


Abnormal Osmolarity is defined by:

- Osmolarity (in either eye) is **greater than 300 mOsm/L**, delineating a normal from a mild/moderate dry eye population
- **OR**, when the inter-eye difference is greater than 8 mOsm/L, indicating instability of the tear film



ABNORMAL VS. NORMAL PATIENT RESULTS

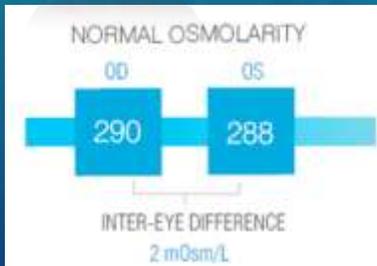


Now that we know what these numbers mean, what do we do with them?

Diagnose
Manage



NORMAL TEAR OSMOLARITY TEST IN SYMPTOMATIC PATIENTS



Methods:

- Prospective observational study of 50 patients
- One or more symptoms of potential DED
- Normal tear osmolarity (<308 mOsm/L in each eye, and an inter-eye difference <8 mOsm/L)

Reference: Ashley R. Brissette; Kelley J. Bohm; Christopher E. Starr.
Weill Cornell Medical College Presented at the Tear Film and Ocular Surface Society Conference, 2016



NORMAL TEAR OSMOLARITY TEST IN SYMPTOMATIC PATIENTS

Results:

Mean tear osmolarity = 293.3 mOsm/L (+/- 6.7)

Mean inter-eye difference = 0.94 mOsm/L (+/- 3.18)

- Allergic conjunctivitis (24%)
- Anterior blepharitis (24%)
- EBMD (12%)
- Keratoneuralgia (12%)
- Contact lens intolerance (8%)
- Conjunctivochalasis (8%)
- Computer vision syndrome (6%)
- Trichiasis (6%)
- Dry eye disease with effective therapy (4%)

Reference: Presented at the Tear Film and Ocular Surface Society Conference, 2016



NORMAL TEAR OSMOLARITY TEST IN SYMPTOMATIC PATIENTS

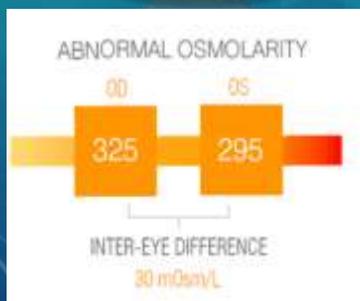
Conclusions:

- Common dry eye disease symptoms overlap significantly with a wide variety of diseases
- If tear osmolarity is normal, use the exam and other diagnostic tools to find alternate diagnosis
- Most common diagnoses were allergic conjunctivitis, anterior blepharitis and corneal EBMD
- Patients may be under topical/systemic treatment

Reference: Presented at the Tear Film and Ocular Surface Society Conference, 2016



ABNORMAL TEAR OSMOLARITY TEST IN ASYMPTOMATIC PATIENTS





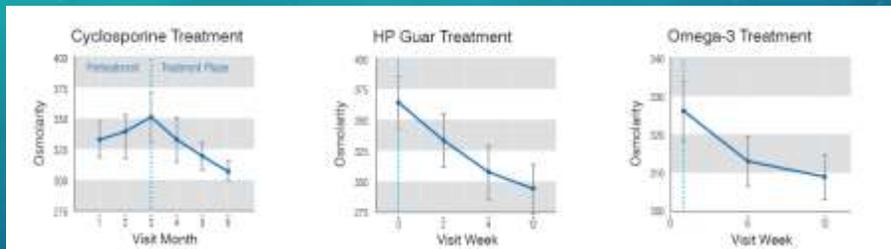
ABNORMAL TEAR OSMOLARITY TEST IN ASYMPTOMATIC PATIENTS

Conclusions:

- Early diagnosis of DED, progression to symptoms and signs will occur sooner or later
- Late diagnosis of DED, corneal nerves have been damaged



MANAGE THERAPEUTIC RESPONSE: ABNORMAL OSMOLARITY DECREASES WITH EFFECTIVE TREATMENT



- Customize your treatment plan based on severity
- Use osmolarity quantitative data to manage patient progress

- Sullivan BD, Crews LA, Sönmez B, et al. Clinical utility of objective tests for dry eye disease: variability over time and implications for clinical trials and disease management. *Cornea*. Sept 2012;31(9): 1000-1008.

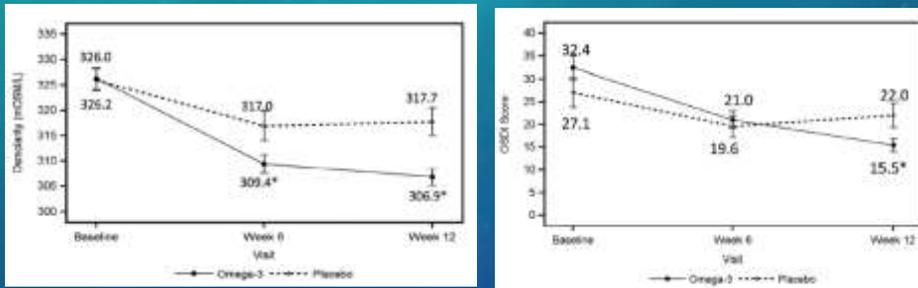
- Gómez AT, et al. Effects of lubricating agents with different osmolalities on tear osmolarity and other tear function tests in patients with dry eye. *Curr Eye Res*. Nov 2013; 38(11): 1095-1103.

- Epitropoulos A, Donnenfeld E, et al. Effect of oral re-esterified omega-3 nutritional supplementation on dry eyes. *Cornea*. Sept 2016; 35 (9): 1185-1191.

MANAGE THERAPEUTIC RESPONSE: OMEGA-3 NUTRITIONAL SUPPLEMENTATION



- Multicenter, prospective, placebo-controlled, double-masked study
- 105 subjects completed the study. They were randomized to omega-3 (n = 54) and control group (n = 51).
- Subjects measured at baseline, week 6 and week 12 with tear osmolarity reduction as primary objective



The omega-3 treatment group had a significant decrease in tear film osmolarity at 6 weeks ($P = 0.042$) and 12 weeks ($P = 0.004$).

Epitropoulos A, Donnenfeld E, et al. Effect of oral re-esterified omega-3 nutritional supplementation on dry eyes. *Cornea*. Sept 2016; 35 (9): 1185-1191.

CLINICAL TAKEAWAYS



- Osmolarity is an important biomarker of ocular surface health.
- Dry Eye Workshop (DEWS) definition of dry eye disease : 'The core mechanisms of dry eye are driven by tear hyperosmolarity and tear film instability'.
- Abnormal osmolarity indicates an unhealthy tear film, which can potentially damage the ocular surface and cornea.
- Abnormal osmolarity is defined by:
 - Osmolarity is greater than 300 mOsm/L , OR , when the inter-eye difference is greater than 8 mOsm/L
- If tear osmolarity is normal in a symptomatic patient, It may not be dry eye.
- Diagnose: Test both eyes to uncover if tear osmolarity is abnormal or normal.
- Manage therapeutic response: Abnormal osmolarity decreases with effective treatment.