

The logo features a stylized blue and green water droplet icon to the left of the text. The text 'TearLab' is in a large, bold, blue sans-serif font, with a trademark symbol (TM) to its upper right. Below it, 'Osmolarity System' is written in a smaller, blue, italicized sans-serif font.

TearLabTM
Osmolarity System



LITERATURE REVIEW

TITLE, AUTHORS, REFERENCE (Quality of evidence ^a / country of study)	BACKGROUND / STUDY DETAILS	KEY FINDINGS / RELEVANCE TO TEARLAB
<p>Methodologies to diagnose and monitor dry eye disease.</p> <p>2007 Report of the International Dry Eye Workshop (DEWS). <i>The Ocular Surface</i> 2007;5(2):65-204. (Level 1 / International)</p>	<ul style="list-style-type: none"> ■ The DEWS Diagnostic Methodology Subcommittee created a detailed database of current tests used to screen, diagnose and monitor DED. ■ Tests for the diagnosis and monitoring of DED were recommended based on their quality and practicality in a general clinic. 	<ul style="list-style-type: none"> ■ In general, with some exceptions, there is still a deficiency of adequately validated symptom questionnaires and objective tests. ■ Tear osmolarity measurement is probably the single most important objective test in DED diagnosis because: <ul style="list-style-type: none"> — it is a parameter that is directly involved in the mechanism of dry eye — the recommended diagnostic cutoff of >316 mOsm/L has been well validated (see next publication) ■ <i>“The way forward will be with new, minimally invasive techniques [e.g., TearLab] that sample the eye and preserve its steady state.”</i>
<p>Tear film osmolarity: determination of a referent for dry eye diagnosis.</p> <p>Tomlinson A, Khanal S, Ramaesh K, Diaper C, McFadyen A. <i>Invest Ophthalmol Vis Sci</i> 2006;47:4309-4315. (Level 2 / UK)</p>	<ul style="list-style-type: none"> ■ A meta-analysis of 17 published tear osmolarity studies in normal and dry eyes to: <ul style="list-style-type: none"> — determine new referents (cutoff values) for tear film hyperosmolarity in the diagnosis of KCS — assess the effectiveness of the cutoff values in independent patient groups 	<ul style="list-style-type: none"> ■ The study provided a well-validated cutoff value for tear hyperosmolarity of 316 mOsm/L. ■ The 316 mOsm/L value accurately diagnosed dry eye in 89% of cases. ■ This degree of accuracy was superior to any other single test for dry eye diagnosis (Lactoplate, Schirmer test, and Rose Bengal staining), and comparable with the results of combined tests. ■ <i>“Measurement of tear osmolarity is a powerful tool in the diagnosis of KCS and has the potential to be accepted as the gold standard for the disease. The advent of new technology, making clinical testing of this feature of tear physiology simple, practical and inexpensive, could provide the impetus to its adoption in the diagnosis of KCS.”</i>
<p>Assessment of tear film dynamics: quantification approach.</p> <p>Tomlinson A, Khanal S. <i>The Ocular Surface</i> 2005;3:81-95. (Level 3 / UK)</p>	<ul style="list-style-type: none"> ■ A review of the quantitative assessment of those aspects of tear film dynamics that can be fully and directly measured 	<ul style="list-style-type: none"> ■ Tear turnover rate (by fluorophotometry), tear film evaporation (by evaporimetry) and tear osmolarity (by FPD) give the most direct and quantifiable measures of tear film dynamics available to date but all techniques are difficult to perform, expensive and time-consuming. ■ Measurement of tear osmolarity using Clifton nanometer FPD osmometer is currently accepted as the “gold standard” for DED diagnosis but technical difficulties mean that considerable expertise is needed to obtain consistent results. ■ <i>“A measure of tear film osmolarity by a rapid and less expertise-dependent technique [than the Clifton osmometer] must await development of new clinically applicable instruments. Such instruments are in development but are not currently available...”</i>

TITLE, AUTHORS, REFERENCE (Quality of evidence ^a / country of study)	BACKGROUND / STUDY DETAILS	KEY FINDINGS / RELEVANCE TO TEARLAB
<p>Osmolarity of tear microvolumes in keratoconjunctivitis sicca.</p> <p>Gilbard JP, Farris RL, Santa Maria II J. <i>Arch Ophthalmol</i> 1978;96:677-681. (Level 2 / USA)</p>	<ul style="list-style-type: none"> ■ Study to evaluate tear film osmolarity as a diagnostic tool for KCS, and the possible role of elevated tear film osmolarity in the disorder's pathogenesis. ■ Tear film samples were obtained from 31 normal eyes (36 samples) and 30 KCS eyes (38 samples) using a new technique that virtually eliminated problems of reflex tearing and sample evaporation, and osmolarity was measured using FPD. 	<ul style="list-style-type: none"> ■ Mean (\pm SD) tear osmolarity in normal and KCS eyes was 302 (\pm 6.3) and 343 (\pm 32.3) mOsm/L, respectively ■ The sensitivity and specificity of a single measurement were 94.7% and 93.7%, respectively ■ <i>This landmark study showed the value of tear film osmolarity measurement as a diagnostic tool for KCS and highlighted the importance of using a sampling technique that minimizes reflex tearing and sample evaporation</i>
<p>Tear osmolarity variation in the dry eye</p> <p>Farris L, Stuchell R, Mandel ID. <i>Trans Am Ophthalmol Soc</i> 1986;84: 250-268. (Level 2 / USA)</p>	<ul style="list-style-type: none"> ■ Study evaluating variations of tear osmolarity in KCS patients and in age- and sex-matched normal volunteers (the control group). ■ Samples were obtained using a technique that minimizes reflex tearing, sample evaporation and contamination, and osmolarity was measured using FPD. 	<ul style="list-style-type: none"> ■ Mean tear osmolarity results showed that values were: <ul style="list-style-type: none"> — significantly higher among KCS patients than control subjects; 324 (\pm 11) vs. 303 (\pm 5) mOsm/L ($p < 0.001$) — not significantly affected by gender or by eye (right vs. left) in either KCS patients or normal controls — significantly higher in the afternoon than the morning among normal individuals; 308 vs. 305 ($p < 0.01$) ■ Elevated lactoferrin concentrations in basal and reflex tears correlated significantly with the severity of KCS as determined by increased tear osmolarity ■ <i>The study confirmed the value of tear osmolarity in KCS diagnosis</i>
<p>Dry eye diagnosis</p> <p>Khanal S, Tomlinson A, McFadyen A, Diaper C, Ramaesh K. <i>Invest Ophthalmol Vis Sci</i> 2008;49: 1407-1414. (Level 2/UK)</p>	<ul style="list-style-type: none"> ■ Study to determine the most effective, objective test for diagnosis of dry eye disease ■ Forty-one patients with dry eye and 32 normal patients were assessed for symptom, tear film quality, evaporation, tear turnover rate (TTR), osmolarity and meibomian gland dropout 	<ul style="list-style-type: none"> ■ Eyes with dry eye disease had TTR, tear evaporation and osmolarity levels that were significantly different from normal eyes ■ The study found that tear osmolarity is the best single test for diagnosis of dry eye disease, with an overall accuracy of 79% ■ The combination of TTR, tear evaporation and osmolarity was most effective, with an overall accuracy of 89% ■ <i>If a single dry eye diagnostic test is used, tear osmolarity is the most accurate option for diagnosis</i>

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<p>Prevalence of dry eye syndrome among US women.</p> <p>Schaumberg DA, Sullivan DA, Buring JE, Dana MR.</p> <p><i>Am J Ophthalmol</i> 2003;136:318-326.</p> <p>(Level 1 / USA)</p>	<ul style="list-style-type: none"> DES is believed to be one of the most common ocular problems in the USA, particularly among older women, but few studies have investigated the magnitude of the problem in women and how this may vary with demographic characteristics. This cross-sectional prevalence survey evaluated DES and dry eye symptoms in 39,876 US women participating in the Women's Health Study. DES was defined as the presence of clinically diagnosed DES or severe symptoms (both dryness and irritation constantly or often). 	<ul style="list-style-type: none"> DES leading to a clinical diagnosis or severe symptoms is prevalent, affecting over 3.2 million American women middle-aged and older. DES prevalence increased with age: 5.7% in pre-menopausal women (aged <50 years) to 9.8% in women aged >75 years. Although the condition is more prevalent among older women, it also affects many in their 40s and 50s. <i>Results highlight that DES is a major public health problem (affecting QOL and healthcare resources) – this will undoubtedly increase due to the aging population.</i>
<p>Tear film, contact lens, and patient-related factors associated with contact lens-related dry eye.</p> <p>Nichols JJ, Sinnott LT.</p> <p><i>Invest Ophthalmol Vis Sci</i> 2006;47:1319-1328.</p> <p>(Level 2 / USA)</p>	<ul style="list-style-type: none"> Cross-sectional study in 415 contact lens wearers to examine tear film, type of contact lens, medical-, and patient-related factors associated with self-reported contact lens-related dry eye. Data from 360 patients were analyzed. NB. Tear film osmolarity was measured using an osmometer (Advanced Instruments, Inc.). 	<ul style="list-style-type: none"> Multivariate modeling showed that dry eye status was related to female gender (p=0.007), lenses with higher nominal water content (p=0.002), rapid prelens tear film thinning time (p=0.008), frequent use of over-the-counter pain medication (p=0.02), limbal injection (p=0.03) and increased tear film osmolarity (p=0.05). <i>“Contact lens-related dry eye may be explained mechanistically by increased tear film thinning times (evaporation or rewetting) resulting in increased tear film osmolality.”</i>
<p>Is osmolarity a key feature in dry eye in postmenopausal women?</p> <p>Nichols KK, Jones LA.</p> <p>ARVO 2008, Poster number D726.</p> <p>(Level 2 / USA)</p>	<ul style="list-style-type: none"> Study of 500 post-menopausal women with dry eye in which osmolarity (measured using the Advanced Instrument, Inc., osmometer) as well as other objective tests and patient-reported data were evaluated. 	<ul style="list-style-type: none"> Unlike osmolarity in contact lens dry eye (Nichols et al., 2006 – see publication above), there was no association with the disease in this study; the authors considered this may be due to difficulties in sample collection and transfer. <i>“Newer osmolarity technology may improve sample collection and result in better data from patients with more significant dry eye.”</i>



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7,017,394; 7,051,569; 7,111,502;
7,129,717; 7,204,122

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DES, dry eye syndrome; KCS, keratoconjunctivitis sicca; QOL, quality of life; DED, dry eye disease; FPD, freezing point depression
a. The quality of the data (level of evidence) was based on the Evidence Grading Scheme contained in the DEWS Report and based on the American Academy of Ophthalmology Preferred Practice Pattern Series (page 163).

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