

CHAPTER 1

THE DIAGNOSIS OF DRY EYE: CLASSIC VERSUS THE CONTEMPORARY

Arzu TAŞKIRAN ÇÖMEZ ¹

Aslı KAHRAMAN ²

INTRODUCTION

Dry eye is defined as a multifactorial disorder in which homeostatic loss occurs through a complex etiology, leading to tear film instability associated with hyperosmolarity, inflammation, ocular surface damage, and neurosensory abnormalities, as stated in TFOS II in 2017 (1,2,3). In the same year, the Asian Dry Eye Society proposed an alternative description: “Dry eye is a multifactorial disease characterized by unstable tear film causing a variety of symptoms and/or visual impairment, potentially accompanied by ocular surface damage” (3).

The prevalence of dry eye has been reported between 5 and 50%, with rates increasing up to 75% among the elderly and being consistently higher in women compared with men (4-7).

As a chronic condition, DED causes discomfort and impairs visual acuity, daily activities, and occupational performance, thereby reducing overall quality of life (5-6).

Approximately 10% of patients present with the aqueous-deficient form, while the remaining 90% exhibit evaporative disease or a mixed phenotype. Apart from age-related decline in lacrimal gland secretion, multiple etiological contributors are recognized: female sex, smoking, ethnicity, systemic or topical medications (including antihypertensives, anticholinergics, antiglaucoma drugs, and retinoic acid), systemic disorders such as diabetes mellitus, rheumatoid arthritis, Sjögren

¹ Prof. Dr., University of Health Sciences, Prof.Dr.Cemil Tascioglu City Hospital, Department of Ophthalmology arzucomez@yahoo.com, ORCID iD: 0000-0001-8048-8146

² MD, University of Health Sciences, Prof.Dr.Cemil Tascioglu City Hospital, Department of Ophthalmology aslikahraman27@icloud.com, ORCID iD: 0009-0000-1518-7283

REFERENCES

1. Nelson JD, Craig JP, Akpek E, Azar DT, Belmonte C, Bron AJ et al. TFOS DEWS II introduction. *Ocul. Surf.* 2017; 15: 269–275.
2. Craig JP, Nichols KK, Akpek EK, Caffery B, Dua HS, Joo CK, Liu Z, Nelson JD, Nichols JJ, Tsubota K, Stapleton F. TFOS DEWS II Definition and Classification Report. *Ocul Surf.* 2017 Jul;15(3):276-283. doi: 10.1016/j.jtos.2017.05.008. Epub 2017 Jul 20. PMID: 28736335.
3. Tsubota K, Yokoi N, Watanabe H, Dogru M, Kojima T, Yamada M, Kinoshita S, Kim HM, Tchah HW, Hyon JY, Yoon KC, Seo KY, Sun X, Chen W, Liang L, Li M, Tong L, Hu FR, Puangsricharn V, Lim-Bon-Siong R, Yong TK, Liu Z, Shimazaki J; Members of The Asia Dry Eye Society. A new perspective on dry eye classification: Proposal by the Asia Dry Eye Society. *Eye Contact Lens.* 2020 Jan;46 Suppl 1:S2-S13. doi:10.1097/ICL.0000000000000643
4. Stapleton F, Alves M., Bunya V. Y., Jalbert I., Lekhanont K., Malet F, Jones L. (2017). TFOS DEWS II Epidemiology Report. *The Ocular Surface*, 15(3), 334–365. doi:10.1016/j.jtos.2017.05.003
5. Farrand KF, Fridman M, Stillman IO, Schaumberg DA. Prevalence of Diagnosed Dry Eye Disease in the United States Among Adults Aged 18 Years and Older. *Am J Ophthalmol* 2017;182:90–98.
6. Pflugfelder SC. Prevalence, burden, and pharmacoeconomics of dry eye disease. *Am J Manag Care.* 2008;14(3 Suppl):S102–106.
7. Gomes JAP, Azar DT, Baudouin C, Efron N, Hiramaya M, Horwath-Winter J, Wolffsohn JS. TFOS DEWS II Iatrogenic Report. *Ocul Surf.* 2017;15(3):511–538. doi:10.1016/j.jtos.2017.05.004
8. Milner MS, Beckman KA, Luchs JJ, Allen QB, Awdeh RM, Berdahl J, Boland TS, Buznego C, Gira JP, Goldberg DE, Goldman D, Goyal RK, Jackson MA, Katz J, Kim T, Majmudar PA, Malhotra RP, McDonald MB, Rajpal RK, Raviv T, Rowen S, Shamie N, Solomon JD, Stonecipher K, Tauber S, Trattler W, Walter KA, Waring GO 4th, Weinstock RJ, Wiley WF, Yeu E. Dysfunctional tear syndrome: dry eye disease and associated tear film disorders - new strategies for diagnosis and treatment. *Curr Opin Ophthalmol.* 2017 Jan;27 Suppl 1(Suppl 1):3-47. doi: 10.1097/01.icu.0000512373.81749.b7.
9. Sullivan DA, Rocha EM, Aragona P, Clayton JA, Ding J, Golebiowski B, Hampel U, McDermott AM, Schaumberg DA, Srinivasan S, Versura P, Willcox MDP. TFOS DEWS II Sex, Gender, and Hormones Report. *Ocul Surf.* 2017 Jul;15(3):284-333. doi:10.1016/j.jtos.2017.04.001. PMID: 28736335.
10. Lemp MD, Baudouin C, Baum J, Dogru M, Foulks GN, Shigeru K, et al. The definition and classification of dry eye disease: report of the definition and classification subcommittee of the international Dry Eye Workshop. *Ocular Surface.* 2007;5(2):75–92.
11. Van Bijsterveld OP. Diagnostic tests in the Sicca syndrome. *Arch Ophthalmol* 1969;82:10e4.
12. Holly FJ, Lemp MA. Tear physiology and dry eyes. *Surv Ophthalmol.* 22: 69– 87, 1977. 21.Sullivan BD, Whitmer D, Nichols KK, Tomlinson A, Foulks GN, Geerling G, et al. An objective approach to dry eye disease severity. *Invest Ophthalmol Vis Sci.* 2010; 51:6125–6130.
13. Begley CG, Chalmers RL, Abetz L, Venkataraman K, Mertzani P, Caffery BA, Snyder C, et al. The relationship between habitual patient- reported symptoms and clinical signs among patients with dry eye of varying severity. *Invest Ophthalmol Vis Sci.* 2003; 44: 4753–4761.
14. Fuentes-Paez G, Herreras JM, Cordero Y, Almaraz A, González MJ, Calonge M. Lack of concordance between dry eye syndrome questionnaires and diagnostic tests. *Arch Soc Esp Ophthalmol.* 2011; 86: 3–7.
15. Bron AJ, de Paiva CS, Chauhan SK, Bonini S, Gabison EE, Jain S, Knop E, Markoulli M, Ogawa Y, Perez VL, Uchino Y, Yokoi N, Zoukhri D, Sullivan DA. TFOS DEWS II Pathophysiology Report. *Ocul Surf.* 2017 Jul;15(3):438-510. doi:10.1016/j.jtos.2017.05.011.
16. Bron, A.J. The definition and classification of dry eye disease. In *Dry Eye*; Springer: Berlin, Germany, 2015; pp. 1–19.
17. Benitez-del-Castillo JM, Lemp MA. *Ocular Surface Disorders: Diagnosis and Medical Management.* JP Medical Publishers; London, UK: 2013. ISBN: 9781907816605.

18. Nelson JD, Craig JP, Akpek EK, Azar DT, Belmonte C, Bron AJ, Clayton JA, Dogru M, Dua HS, Foulks GN, Gomes JAP, Hammit KM, Hodges RR, Koh S, Liu Z, Perry HD, Schaumberg DA, Sullivan DA, Willcox MDP, Zierhut M. TFOS DEWS II Introduction. *Ocul Surf*. 2017 Jul;15(3):269-275. doi:10.1016/j.jtos.2017.05.005. PMID: 28736335.
19. Ding C, Tóth-Molnár E, Wang N, Zhou L. Lacrimal Gland, Ocular Surface, and Dry Eye. *J Ophthalmol*. 2016;2016:7397694. doi: 10.1155/2016/7397694.
20. Prydal, JI, Campbell FW. Study of precorneal tear film thickness and structure by interferometry and confocal microscopy. *Invest. Ophthalmol. Vis. Sci*. 1992, 33, 1996–2005.
21. The definition and classification of dry eye disease: report of the Definition and Classification Subcommittee of the International Dry Eye WorkShop (2007). *Ocul Surf*. 2007 Apr;5(2):75-92. doi: 10.1016/s1542-0124(12)70081-2.
22. Georgiev GA, Yokoi N, Ivanova S, Tonchev V, Nencheva Y, Krastev R. Surface relaxations as a tool to distinguish the dynamic interfacial properties of films formed by normal and diseased meibomian lipids. *Soft Matter*. 2014 Aug 14;10(30):5579-88. doi: 10.1039/c4sm00758a.
23. Millar TJ, Schuett BS. The real reason for having a meibomian lipid layer covering the outer surface of the tear film – a review. *Exp Eye Res*. 2015 Sep;137:125-138. doi:10.1016/j.exer.2015.05.017.
24. Rantamäki AH, Javanainen M, Vattulainen I, Holopainen JM. Do lipids retard the evaporation of the tear fluid? *Invest Ophthalmol Vis Sci*. 2012 Sep 21;53(10):6442-7. doi: 10.1167/iov.12-10487.
25. de Souza GA, de Godoy LM, Mann M. Identification of 491 proteins in the tear fluid proteome reveals a large number of proteases and protease inhibitors. *Genome Biol*. 2006;7(8):R72. doi:10.1186/gb-2006-7-8-r72.
26. Schirmer OWA. *Handbuch der gesamten Augenheilkunde: Mikroskopische Anatomie und Physiologie der Tränenorgane*. Springer; Berlin, Germany: 1931.
27. Nagataki S, Mishima S. Pharmacokinetics of instilled drugs in the human eye. *Int Ophthalmol Clin*. 1980 Summer;20(2):33-49. doi:10.1097/00004397-198002020-00006.
28. Craig JP, Tomlinson A. Importance of the lipid layer in human tear film stability and evaporation. *Optom Vis Sci*. 1997 Jan;74(1):8-13. doi:10.1097/00006324-199701000-00017.
29. Goto E, Tseng SCG. Differentiation of lipid tear deficiency dry eye by kinetic analysis of tear interference images. *Arch Ophthalmol*. 2003 Feb;121(2):173-180. doi:10.1001/archophth.121.2.173.
30. Moss SE, Klein R, Klein BE. Prevalence of and risk factors for dry eye syndrome. *Arch Ophthalmol*. 2000;118(9):1264-1268.
31. Gayton JL. Etiology, prevalence, and treatment of dry eye disease. *Clin Ophthalmol*. 2009;3:405-412.
32. Ozawa Y, Kawashima M, Inoue S, Suzuki T, Shimizu S, Tsubota K. Dry eye disease and anticholinergic burden. *Sci Rep*. 2023;13(1):12847.
33. Ngo W, Situ P, Keir N, Korb D, Blackie C, Simpson T. Psychometric properties and validation of the Standard Patient Evaluation of Eye Dryness questionnaire. *Cornea*. 2013 Sep;32(9):1204-1210. doi:10.1097/ICO.0b013e318294b0c0.
34. 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):615-621. doi:10.1001/archophth.118.5.615.
35. Chalmers RL, Begley CG, Caffery B. Validation of the 5-Item Dry Eye Questionnaire (DEQ-5): Discrimination across self-assessed severity and aqueous tear deficient dry eye diagnoses. *Cont Lens Anterior Eye*. 2010 Apr;33(2):55-60. doi:10.1016/j.clae.2009.12.010.
36. Amparo F, Schaumberg DA, Dana R. Comparison of Two Questionnaires for Dry Eye Symptom Assessment: The Ocular Surface Disease Index and the Symptom Assessment in Dry Eye. *Ophthalmology*. 2015;122(7):1498–503. 60. doi:10.1016/j.clae.2009.12.010
37. Messmer EM. The pathophysiology, diagnosis, and treatment of dry eye disease. *Dtsch Arztebl Int*. 2015 Jan 30;112(5):71-81; quiz 82. doi: 10.3238/arztebl.2015.0071.

38. Milner MS, Beckman KA, Luchs JJ, Allen QB, Awdeh RM, Berdahl J, Boland TS, Buznego C, Carlson AN, Deepinder D, Donnenfeld ED, Dunaief JL, Farid M, Finch DR, Fowler G, Friend J, Goldberg DF, Goyal RK, Guggenheim CJ, Holland EJ, Huynh K, Kahook MY, Katz J, Kim T, Majmudar PA, Malhotra RP, McDonald MB, McDonald T, Melton R, Nelson JD, Nichols KK, Nijm LM, O'Brien TP, Park J, Pflugfelder SC, Rapuano CJ, Rowen S, Shamie N, Sheppard JD Jr, Smith J, Solomon R, Stonecipher KG, Tauber J, Trattler W, Tseng SC, Vold S, Walters T, Weinstein RJ, Yeu E. Dysfunctional tear syndrome: dry eye disease and associated tear film disorders – new strategies for diagnosis and treatment. *Curr Opin Ophthalmol*. 2017 Jan;27 Suppl 1:3-47. doi:10.1097/01.icu.0000512373.81749.b7.
39. Mooi JK, Wang MT, Lim J, Müller A, Craig JP. Minimising instilled volume reduces the impact of fluorescein on clinical measurements of tear film stability. *Cont Lens Anterior Eye*. 2017; 40:170-174.
40. Hirji N, Patel S, Callander M. Human tear film pre-rupture phase time (TP-RPT) -a non-invasive technique for evaluating the pre-corneal tear film using a novel keratometer mire. *Ophthal Physiol Opt*. 1989;9:139e42.
41. Loveridge R. Breaking up is hard to do? *Optometry Today*, 1993; 18-24. 7. Hirji N, Patel S and Callender M. Human tear film pre-rupture phase time (TP-RPT): a non-invasive technique for evaluating the pre-corneal tear film using a novel keratometer wire. *Ophthal Physiol Opt*. 1989; 9:4 139-142.
42. Lemp MA. Advances in understanding and managing dry eye disease. *Am J Ophthalmol*. 2008 Sep;146(3):350-356. doi:10.1016/j.ajo.2008.05.016.
43. Sambursky R, Davitt WF 3rd, Latkany R, Tauber S, Starr C, Friedberg M, Dirks MS, McDonald M. Sensitivity and specificity of a point-of-care matrix metalloproteinase 9 immunoassay for diagnosing inflammation related to dry eye. *Br J Ophthalmol*. 2014 Feb;98(2):152-7. doi: 10.1136/bjophthalmol-2013-303468. PMID: 24106164.
44. Chotikavanich S, de Paiva CS, Li DQ, Chen JJ, Bian F, Farley WJ, Pflugfelder SC. 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. doi: 10.1167/iovs.08-2476