Dry Eye Symptomatology and Pathophysiology: New Understandings

Kelly K. Nichols, OD, MPH, PHD, FAAO

A remarkable increase in our knowledge about dry eye has led to many new developments in the field, but proper management of this common ocular surface disease still begins with thoughtful symptom queries and recognition of underlying causes.

Since the 2007 international Dry Eye Workshop (DEWS), enormous advances have occurred in the understanding and management of dry eye disease (DED). So substantial has been the progress that a second DEWS has taken place. The TFOS DEWS II report, published in 2017, is a summary of the last 10 years’ worth of effort in clinical and basic DED research and knowledge. Most importantly, it has outlined new recommendations that will help advance our efforts in improving patient care.

As with any disease, having a good grasp of DED’s symptomatology and pathophysiology will help practitioners better diagnose and treat patients. Though highly prevalent, DED is often overlooked in clinical practice or not reported by patients. To improve management of the disease, it is important for practitioners to first assess symptoms and then analyze test findings to identify the root cause, which can vary from patient to patient.

Symptom Assessment

DED patients may experience a variety of symptoms: discomfort, blurred vision, dryness, irritation, and, in some cases, just awareness of their eyes. These ocular surface symptoms are nonspecific and often not self-reported. To identify suspect DED and establish the need for further assessment, a good first step is to ask patients how their eyes feel and what kind of symptom triggers they experience (eg, environmental or certain medications).

The TFOS DEWS II report recommends an initial symptom survey be conducted using the Ocular Surface Disease Index (OSDI) or the 5-item Dry Eye Questionnaire (DEQ-5). Both DED questionnaires are relatively short and ask questions about eye irritation, dryness, and visual changes. The questionnaire can be administered by staff at the beginning of a visit. Then, when interacting with a patient, the eye care provider can encourage him or her to talk more about any symptoms by asking how often the symptoms occur, when they occur, and whether they impact the patient’s daily activities.

Signs and Symptoms

DED symptoms correlate poorly with clinical signs, and clinical tests for DED often lack correlation with one another.2-4 Taking this into consideration, the TFOS DEWS II definition and classification committee has developed a patient-centric DED classification scheme that starts with the assessment of symptoms and is followed by a review of clinical signs.5 Based on the presence or absence of relevant symptoms and signs, the classification scheme differentiates presenting patients into four categories: symptomatic with signs, symptomatic without signs, asymptomatic with signs, and asymptomatic without signs.

Patients who are symptomatic but show no evident clinical signs might not have DED, but it is more likely that they have early, pre-clinical disease. DED

TARGET AUDIENCE This educational activity is intended for optometrists.

LEARNING OBJECTIVES Upon completion of this activity, participants will be able to:
1. Use the patient-centric classification scheme to guide clinical decisions in the diagnosis and treatment of DED.
2. Outline the core mechanisms and the vicious inflammatory circle that underlie the initiation and perpetuation of DED.
3. Understand the role of the meibomian glands in ocular surface health and disease.
4. Better assess meibomian structure and function in everyday practice.

Key Issues in Ocular Surface Disease is sponsored by New England College of Optometry and supported by an unrestricted educational grant from Shire. This publication is administered by an independent editorial committee.

© 2017 Candeeo Clinical/Science Communications, LLC. All rights reserved. Neither New England College of Optometry nor Candeeo Clinical/Science Communications, LLC, assumes any responsibility for injury or damage to persons or property arising from the use of information or ideas contained in this publication.

COURSE DIRECTOR Tony Cavallerano, OD, FAAO, New England College of Optometry, Boston, MA, USA

Also in this Issue:
Examination and Imaging for Dry Eye Disease Evaluation
Katherine M. Mastrota, MS, OD, FAAO
2

Key Issues in Ocular Surface Disease

in the initial stage can be very variable. The snapshot provided by one eye exam in the office cannot capture the state of the ocular surface all the time. This may explain in part the variability of clinical signs for DED. The lack of signs in symptomatic patients, therefore, could mean that they either have not taken the right tests or simply are having a good day in terms of their DED.

Conversely, patients with DED may exhibit signs of ocular surface disease but no symptoms. Often, these are patients who have suffered chronic, longstanding disease and, as a result, have neurotrophic keratopathy. Their symptoms, masked by the reduced corneal sensitivity, can manifest unexpectedly as the ocular surface improves with treatment. The lack of symptoms can also be a sign that patients have become used to the way their eyes feel. I have heard patients say, “I really didn’t realize how bad my eyes felt until they started feeling better.” Even patients with significant DED may describe their eyes as feeling “just fine.” When queried more in-depth, however, these patients often will bring up some symptoms they are experiencing—even visual symptoms—the problem is not that they have none of the symptoms of DED; rather, it is the chronicity of the disease that has led them to feel accustomed to the level of ocular discomfort or visual disturbance they routinely experience.

Diagnosing Dry Eye

Diagnosing DED can be complicated. The general recommendation is to query symptoms and keep an open mind when going through diagnostic testing. If a patient is confirmed to have symptoms (DEQ-5 ≥ 6 or OSDI ≥ 13), then the initial diagnosis of DED can be made when one of the following three tests is positive: tear breakup time (TBUT), tear osmolarity, and ocular surface staining. Other ocular surface diseases may present with symptoms and signs that mimic DED. The use of triaging questions may aid in the differential diagnosis by indicating where further investigation is warranted.

When there is a discrepancy between signs and symptoms, I tend to put more importance on symptoms. In my experience, as long as symptoms are present, it is worth continuing to manage the patient to collect more data points. In the meantime, it is important to realize that no single test alone can diagnose all DED. Take fluorescein staining: practitioners are trained to look for corneal fluorescein staining in DED, while in fact superficial punctate keratitis is absent in many DED patients and present in some normal individuals at any given time. To refine a DED diagnosis, a combination of different tests is necessary.

Many DED patients are diagnosed when presenting with conditions that

STATEMENT OF NEED

Although dry eye is often used as a synonym for dry eye disease, the term “ocular surface disease” refers to a cluster of anterior eye disorders that includes dry eye (evaporative or due to tear insufficiency), bacterial and viral infections, blepharitis, meibomian gland dysfunction, allergic conjunctivitis, ocular surface problems associated with glaucoma treatment, and the ocular manifestation of systemic inflammatory diseases and endocrine disorders [eg, Sjögren’s syndrome, arthritis, and thyroid disease].

While prevalence data vary considerably based on the population studied and disease definition, all of these conditions are common.1-3 In addition, they share pathogenic mechanisms, have overlapping clinical signs and symptoms, and are often comorbid.4 For example, allergic conjunctivitis, blepharitis, and Sjögren’s syndrome—like dry eye disease—are inflammatory conditions that affect the ocular surface and share a number of symptoms, including discomfort, itching, dryness, and irritation.1-4

Diagnosis and treatment of ocular surface disease are clearly important, but they are rendered difficult by a number of factors: the frequency of comorbid conditions with similar signs and symptoms; incomplete understanding of the underlying pathogenesis; frequently poor correlation between signs and symptoms; occasional systemic disease as an underlying factor, and the absence of simple, clear diagnostic tests. Even after diagnosis, adherence to best practice in patient management is complicated by the number of agents available and competing claims for them in the marketplace.

Each installment of Key Issues in Ocular Surface Disease will look at two important topics in the management of ocular surface disease in order to support optometrists’ clinical reasoning and decision-making abilities and navigate the growing body of sometimes contradictory evidence on ocular surface disease. The benefits are substantial: accurate diagnosis and effective treatment of ocular surface disease will contribute greatly to patient comfort and satisfaction, help patients enjoy comfortable contact lens wear, and significantly enhance outcomes in cataract and corneal refractive surgery.

References


OFF-LABEL USE STATEMENT

This work may discuss off-label uses of medications.

GENERAL INFORMATION

This CE activity is sponsored by New England College of Optometry and is supported by an unrestricted educational grant from Shire.

DATE OF ORIGINAL RELEASE

October 2017. Expiration Date: 09-12-2020.

ACCREDITATION STATEMENT

This activity has been planned and implemented through the joint sponsorship of New England College of Optometry and Cardio Clinical/Science Communications, LLC. New England College of Optometry is accredited by The Council on Optometric Practitioner Education® (COPE®), created by the Association of Regulatory Boards of Optometry (ARBO) to accredit continuing education on behalf of optometric licensing boards.

CREDIT DESIGNATION STATEMENT

This Distance Learning CE course is sponsored by New England College of Optometry and is supported by an unrestrictted educational grant from Shire.

DISCLAIMER

Participants have an implied responsibility to use the newly acquired information to enhance patient outcomes and professional development. The information presented in this activity is not meant to serve as a guideline for patient care. Any procedures, medications, or other courses of diagnosis or treatment discussed or suggested in this activity should not be used by clinicians without evaluation of their patients’ conditions and possible contraindications or dangers in use, applicable manufacturer’s product information, and comparison with recommendations of other authorities.

COMERCIAL SUPPORTERS

This activity is supported by an unrestricted educational grant from Shire.

AUTHOR BIOS/DISCLOSURE STATEMENTS

Katherine M. Mastrotta, MS, OD, FAAO, is director of optometry at the NY Hotel Trades Council and Hotel Association of NYC Employee Benefits Fund, Health Center, Inc. She is a consultant for Allergan, Shire, Beaver-Visitec International, and OCuSOFT. Dr. Mastrotta is also a stockholder of TearLab.

Kelly K. Nichols, OD, MPH, PHD, FAAO, is dean of the University of Alabama at Birmingham School of Optometry in Birmingham, AL. Dr. Nichols is a consultant for Allergan, Eleven Biotherapeutics, InSite Vision, Kala Pharmaceuticals, Parion Sciences, Shire, Sun Pharmaceutical Industries Ltd., ScienceBased Health, and Santen. She has also received grant/research support from Eleven Biotherapeutics, Kala Pharmaceuticals, Shire, TearScience, and J&J Vision Care.

To take the test online and obtain CE credit for this activity, go to http://www.neco.edu/academics/continuing-education/online-ce/kiosd
are seemingly unrelated to DED. For example, we now often find DED in patients that are getting ready for cataract surgery. The high prevalence of DED among patients scheduled for cataract surgery has been demonstrated in clinical studies. These patients may not complain of DED—likely because vision and cataract are on top of their mind—but their visual outcomes may suffer without preoperative control of DED.

Following the initial diagnosis, DED can be classified into two primary categories based on etiology: aqueous-deficient dry eye (ADDE) and evaporative dry eye (EDE). In each category, a range of factors may contribute to development of the disease. The current TFOS DEWS II report emphasizes that ADDE and EDE exist on a continuum and often overlap. The majority of DED patients have indeed been found to have the combination type of disease. Following the initial diagnosis of DED, a series of additional tests can be performed to further determine which subtype is predominant, including tear meniscus assessment (measures aqueous volume), a Phenol red thread or Schirmer test (measure aqueous production), and examination of the meibomian glands to assess their overall health and function. Treatment for DED should target the predominant disease subtype—without ignoring other etiological components.

Core Mechanisms

In the TFOS DEWS II report, DED is defined as “a multifactorial disease of the ocular surface characterized by a loss of homeostasis of the tear film, and accompanied by ocular symptoms, in which tear film instability and hyperosmolarity, ocular surface inflammation and damage, and neurosensory abnormalities play etiological roles.” The recognition of the multiple etiological elements involved in DED is a key difference between this new definition and the one in the original DEWS report.

The core mechanisms involved in the initiation and perpetuation of DED, based on current understanding of DED’s pathophysiology, include tear hyperosmolarity, thinning and destabilization of the tear film, and inflammation of the ocular surface. Among these, tear hyperosmolarity is thought to play a central pathogenic role by stimulating a vicious circle of DED in which a cascade of inflammatory responses leads to tissue damage that leads to subsequent inflammation. This vicious inflammatory circle is a common pathway that DED enters regardless of its etiology; it perpetuates the disease and drives its progression. The resulting ocular surface damage would ultimately manifest as corneal staining but may not be visible in early stages, when it occurs largely at the cellular level.

As a multifactorial, complex disease, DED has many aspects to its etiopathophysiology, any one of which can be predominant in a given patient. The unifying feature of the disease, however, is the loss of homeostasis of the tear film. Homeostasis is a term that describes equilibrium and appropriate health of tissues and fluids. For the ocular surface, tear breakup time (TBUT), osmolarity, and vital dye staining are all considered homeostasis markers.

As the fundamental process in the development of DED, disruption of tear film equilibrium can be the result of many changes that occur at the ocular surface in response to various underlying causes of DED. An arid environment and an abnormal lipid layer, for example, could both contribute to increased evaporation and hyperosmolarity of the tear fluid. Neither might necessarily be the initial anomaly, but they can be additive in producing the outward clinical presentation known as DED. The tear film contains a myriad of unique proteins and lipid species that are critical to its function in maintaining a stable, healthy tear film that shows equilibrium. Identifying these molecules will advance our understanding of the various pathways to DED’s pathogenesis.

New Understandings

Neurosensory abnormality has emerged in recent years as the fastest-growing area in DED. The TFOS DEWS II report, with a whole chapter dedicated to the topic of pain and sensation, recognizes neurosensory dysfunction as a feature of DED and a source of discomfort symptoms in patients affected by the disease. The ocular surface inflammation in DED appears to cause sensitization or abnormally increased activity of some sensory nerve terminals (eg, cold thermoreceptors, polymodal nociceptors, and mechano-nociceptors), evoking dryness sensations and pain. This dysfunction of the sensory neurons may account for the lack of consistency between signs and symptoms in some
dry eye patients.

For years, we have been challenged by puzzling cases of DED where patients demonstrate minimum clinical signs upon slit-lamp examination but continue to experience severe symptoms (eg, discomfort, dryness, and burning pain) despite treatment. Recent research suggests that these patients may be suffering chronic neuropathic pain—a condition that involves peripheral and central neural mechanisms—rather than DED.12 Because discomfort and pain are subjective sensations that rely on patients to report, neuropathic pain is difficult to diagnose.

At present, the association between neuropathic pain and DED remains vague. Further exploration is necessary to fully understand neurosensory changes and their significance in DED. Many unanswered questions remain, including how to find these patients and what to do to help them.

Earlier Intervention

Just 10 years ago, DED management in patients presenting for cataract and refractive surgery patients was not even a matter of discussion. Now surgeons have realized how the ocular surface disease is tied to positive surgical outcomes and therefore it is important to treat perioperatively. However, DED remains undermanaged in some other patient groups, such as contact lens wearers. When we hear patients complain that they have to blink to clear their vision with contacts or that they have difficulties wearing the lenses throughout the entire day, patients are often advised that a change in lens material or frequency of replacement will help, as well as a switch in the solutions—without realizing these contact lens-related symptoms might be indicative of underlying DED.

Furthermore, the prevalence of DED is continuing to increase.13 In particular, there is a trend of increasing DED in younger individuals, including school children. This may not be so surprising; an increasing number of cases (eg, young sarcoidosis patients) are being diagnosed. The lack of association between signs and symptoms in patients with dry eye disease, Cornea. 2004;23(8):762-70.

As practitioners we have an obligation to think about prevention and be aware of such potential risk factors as prolonged use of digital devices.

More aggressively managing DED patients may prevent negative outcomes in the long run, and starting treatment early in those who are predisposed to DED may keep them in the state of ocular surface homeostasis longer. Listening carefully to patients’ symptoms can help guide us in that direction, and it is important to consider the patient as a whole: their systemic conditions, the medications they take, if they wear contact lenses or not, their quality of life, and their quality of vision. If there is something that does not sound quite right, then DED should be suspected sooner rather than later.

REFERENCES

To take the test online and obtain CE credit for this activity, go to http://www.neco.edu/academics/continuing-education/online-ce/kiosd
Examination and Imaging for Dry Eye Disease Evaluation

Katherine M. Mastrota, MS, OD, FAAO

A balanced tear film is essential for preventing and correcting meibomian gland-related dry eye disease. Increasingly sophisticated, user-friendly, and affordable imaging options are making routine evaluation of meibomian glands something all eye care providers can do.

Dry eye disease (DED) is one of the most common conditions affecting eye care patients; because signs often precede symptoms, DED is significantly underdiagnosed. Since there is no single test for DED and diagnostic criteria and disease definitions vary widely from study to study, exact prevalence is difficult to pin down. However, according to the recent DEWS II report, which analyzed global data from large, population-based studies, DED prevalence is between 5% and 50% when based on symptoms, and up to 75% when based on signs. The prevalence of meibomian gland dysfunction (MGD)—a leading contributor to DED—is between 38% and 68% among patients over age 40 years. DED symptoms are increasingly being reported in school-aged children and young adults, an alarming trend that is likely related to widespread computer and mobile device use. Looking at digital screens is associated with diminished blink rate, increased interblink interval, and increased proportion of incomplete blinks, all of which increase evaporative tear loss in patients and predispose to DED. According to patient surveys in optometric practice, the average adult between ages 18 and 59 reported spending more than 8 hours per day cumulatively looking at a device, whether a cell phone, tablet, laptop, or desktop computer. Patients in their twenties spent the most time on digital devices, and their OSDI scores were similar to patients in their forties.

Uchino and coworkers showed that prolonged daily work at visual display terminals (at least 8 hours per day) increased DED risk up to 3-fold compared with lesser use. A separate study of 224 consecutive patients (aged 18-78) seen in two optometric practices showed that higher digital device use (more than 2 hours per day) was associated with significantly higher scores on three of four DED questionnaires compared with lower daily digital device use. Almost half of high-usage patients in this study met the OSDI criteria for DED. Further, mean age for the group with worse DED symptoms (ie, the high usage group) was 41 years compared with 53 years in the less affected/lower usage group, suggesting that digital device use might be a more significant risk factor for DED than even the most strongly correlated DED-related factor: age.

DED—including that caused by MGD—can take a tremendous toll on sleep, mood, and other quality of life domains; it has adverse effects on comfort as well as visual function and acuity, contact lens tolerability, and ocular surgical outcomes. Despite this, surveys show that most optometrists do not routinely perform meibomian gland evaluation in everyday practice. All eye care providers should look for opportunities to improve their standard DED and meibomian gland evaluative protocols—filling in gaps in screening, physical examination, and basic tests—and, if not already in place, adding meibography to their diagnostic toolkit.

History, Risk Factors, Comorbidities

Evaluation for DED begins with screening for symptoms via standardized questionnaire or interview; updating information regarding past medical, surgical, and medication histories (ocular and non-ocular); and assessing risk factors for DED and MGD.

Risk factors with good evidence for association with DED include: female sex, older age, Asian ethnicity, presence of MGD, androgen deficiency, computer use, contact lens wear, Sjögren’s or other connective tissue disease, overexposure to polluted or low humidity environments, history of stem cell transplant, and use of certain medications including antihistamines, antidepressants, anxiolytics, and isotretinoin. According to DEWS II (the latest iteration of DEWS), conditions that “probably” increase risk include diabetes; rosacea; allergic conjunctivitis; refractive surgery; and anticholinergic, beta-blocking, and diuretic agents. Patients with a history of sinusitis or migraines may be at increased risk for DED.

An efficient and sensitive way to uncover significant DED comorbidities...
Comprehensive Exam

DEWS II characterizes DED as “a multifactorial disease of the ocular surface characterized by a loss of homeostasis of the tear film and accompanied by ocular symptoms, in which tear film instability and hyperosmolarity, ocular surface inflammation and damage, and neurosensory abnormalities play etiological roles.”13 The emphasis on homeostasis is new and points to an evolving appreciation for the many intricate interwoven elements that culminate in DED—and the responsibility of eye care professionals to identify and characterize this range of contributing factors at early stages.

What constitutes a comprehensive ocular examination for evaluation of DED varies according to each provider’s individual practice, available equipment, and how much of the exam is delegated to assistants or technicians. Despite these variations, what should remain consistent is that the provider: 1) use a systematic approach, and 2) touch on relevant anatomy and major functions of the lacrimal functional unit, including periocular skin, lids (including closure), and lashes; tear volume and spread across the ocular surface; meibomian glands and meibum; and the whole conjunctival and corneal surface. Tear film composition, osmolarity, and inflammatory markers (eg, MMP-9) may also be assessed.14

More detailed descriptions of tests and grading for DED diagnosis are available from numerous sources (AOA,15 AAO,16 Dry Eye Summit,17 and most recently DEWS II,14 to name a few) and are beyond the scope of this article. However, prior to discussing visualization of the meibomian glands, a brief review of manual meibum evaluation seems in order.

Meibomian gland function

By way of review, meibum quality, quantity and expressibility serve as markers for meibomian gland function. Clear oily liquid should be easily expressed from the orifices on the lid margins; thick or cloudy meibum (often described as toothpaste-like), difficulty expressing the glands, or reduced numbers of glands expressed indicate dysfunction (Figure 1).14

Expressing the glands requires no advanced technology and takes little time to perform. However, in the survey of optometrists mentioned above, only 30% of optometrists reported expressing the meibomian glands manually or with an instrument, and only 2% reported using meibography with regularity in their practice.13 A separate study demonstrated that among patients with minimal or no DED symptoms by two screening questionnaires, 60% had meibographic evidence of disease.18

Given that MGD may be present in up to two-thirds of adults18 and that signs frequently do not correlate with symptoms,14 there is a good chance that some (perhaps many) patients in our practices have undiagnosed MGD. More widespread adoption of meibomian gland assessment in everyday practices serves dual functions of helping in the management of the individual patient as well as contributing to our collective knowledge base.

To the latter point, since Korb and colleagues first established a link between the number of functional meibomian glands and DED symptoms, there remains much unexplored terrain relevant to clinical care that might be resolved with more patient data: for example, the range of “normal” meibomian gland appearances; the precise natural history of MGD; roles of acini, gland orifices, and other micro-anatomical features in function and disease; and how gland appearance correlates with function and symptoms.19

Meibomian gland structure

The most basic means for observing meibomian gland structure is simple white light lid transillumination with or without photography. Taking a photograph of the glands aids in visualizing the glands and monitoring changes over time, and it provides a visual aid for communicating with patients in the office about the condition of their glands. From a psychological level, it is not hard to understand how patients who can see concrete evidence of an abnormality may be more inclined to comply with therapy, particularly if they are pre-symptomatic.

Diagnostic Technology

Using an anterior segment camera and monitor to visualize, capture, and optimize ocular images can make the process more efficient and productive for clinician and patient. Slit-lamp digital imaging systems, such as the one I use from TelScreen (TSi Designs, Micro-Med, Inc, Louisville, KY), take high quality...
images under white or infrared light of lid, lash, conjunctiva, and cornea, and do a nice job of illuminating meibomian glands, some tear film characteristics, and surface staining.20

Powerful multi-assessment meibography instruments are available for practitioners seeking a diversity of diagnostic capabilities in a single instrument. LipiView® II Ocular Surface Interferometer (TearScience, Morrisville, NC) captures, stores, and manipulates high quality digital meibographic images using proprietary Dynamic Meibomian Imaging™ technology. It can also evaluate features of the tear film in real time (including sub-micron tear film thickness and tear film response to blinking), other blink dynamics, and aspects of the ocular surface and eyelids including lid closure.21

The Keratograph® 5M (Oculus, Wetzlar, Germany) is a free-standing multidimensional device that offers a unique spectrum of meibographic and tear film assessments in addition to topographic functionality for contact lens fitting (Figure 2). One of the unique features of the Keratograph 5M is its ability to quantify and synthesize five key parameters—conjunctival folds, ocular surface redness, tear meniscus height, non-invasive tear breakup time, and symptoms—and generate a so-called JENVIS DED report. The JENVIS report is comprised of a pair of pentagrams over color-coded DED domains that very clearly lay out patients’ specific deficiencies, which simplifies patient communication and monitoring of disease and response to treatment.22

At least two small portable devices have been developed for dedicated point-of-care high-resolution meibography to appeal to practitioners who want meibography without a large array of other features. LipiScan™ (TearScience, Morrisville, NC) is a standalone unit that utilizes the same near-infrared illumination for meibography as LipiView II.23 The new Meibox Meibographer (Box Medical Solutions, Westlake Village, CA) is designed to attach to a slit lamp so is ultra-portable. Advantages of this system include cloud-based image storage and a lower price point than some competitor products.24

**Conclusion**

The now undeniable role of the meibomian glands and tear film in ocular surface homeostasis and disease makes a thorough assessment of meibomian gland structure and function imperative for providers of comprehensive eye care. Performing manual lid expression more regularly and implementing (or more frequently applying) single-modality or multi-modality meibography in everyday practice will boost awareness and recognition of MGD and DED and provide lifelong value to patients.

---

**Katherine M. Mastrota, MS, OD, FAAO, is the director of optometry at the NY Hotel Trades Council and Hotel Association of NYC Employee Benefits Fund, Health Center, Inc. She is a consultant for Allergan, Shire, Beaver-Visitec International, and OcuSOFT. Dr. Mastrota is also a stockholder of TearLab. Medical writer Noelle Lake, MD assisted in the preparation of this manuscript.**

---

**REFERENCES**

17. Expert Recommendations From The 2014 Dry Eye Summit. Dallas, TX.
18. Schachter A, Schachter S, Hom M. Asymptomatic meibomian gland dysfunction. Poster presented at AAO; April 2016; Seattle WA.
1. Which of the following is a likely diagnosis for patients with significant DED symptoms but no demonstrable signs?
   A. Preclinical dry eye
   B. Neurotrophic keratopathy
   C. Neuropathic pain
   D. A and C

2. According to DEWS II, DED affects what proportion of the adult population?
   A. 5%-50%
   B. 45%-65%
   C. 75%
   D. 95%

3. A meibography device that incorporates a metric for ocular redness into its report is:
   A. LipiView II
   B. LipiScan
   C. Meibox
   D. Keratography 5M

4. Which of the following is NOT a recommended test following symptom assessment for initial diagnosis of DED?
   A. TBUT
   B. Tear osmolarity
   C. Schirmer test
   D. Ocular surface staining

5. Which of the following is a common pathophysiologic component in the vicious circle of DED?
   A. Meibomian gland dysfunction
   B. Ocular surface inflammation
   C. Low tear production
   D. Corneal neurosensory dysfunction

6. Which of the following outcomes have NOT been associated with DED?
   A. Diminished quality of life
   B. Reduced visual acuity
   C. Mood and sleep disturbance
   D. All of the above have been associated with DED

7. Which of the following drugs or drug categories may increase risk for DED?
   A. Antidepressants and anxiolytics
   B. Antihistamines and isotretinoin
   C. A and B
   D. None of the above

8. Which of the following is a recommended tool for symptom screening in the diagnosis of DED?
   A. SPEED survey
   B. OSDI
   C. DEQ-5
   D. B and C

9. Which of the following statements is true about DED symptoms and clinical signs?
   A. They both are variable
   B. Patients with severe DED may not report symptoms
   C. Patients with early disease may not exhibit signs for DED
   D. All of the above

10. Which of the following is NOT a consequence of prolonged digital device use?
    A. Diminished blink rate
    B. Increased interblink interval
    C. Less incomplete blinks
    D. Greater percentage of incomplete blinks