

TAKING AIM AT DRY EYE

How Systematic
Management of this
Chronic Disease is
Improving Patient
Outcomes

A Supplement to

REVIEW
of Ophthalmology

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Taking Aim at Dry Eye

How Systematic Management of this Chronic Disease is Improving Patient Outcomes

The importance of effectively diagnosing and managing dry eye disease (DED) cannot be overstated. We have come to understand that dry eye and ocular surface diseas-

es are chronic and progressive in nature, and that early detection and initiation of treatment is essential for prevention of further advancement.

Many eye care providers now view these diseases in a simi-

lar light as glaucoma, whereby missing the diagnosis can lead to serious, long-term consequences. If not promptly detected and addressed, dry eye can lead to greater risk of eye infection and ocular surface damage, potentially triggering inflammation, corneal abrasion and ulcers, along with vision problems and poor surgical outcomes.¹

Fortunately, awareness of DED has risen among eye care professionals over the last decade.² Patients also are better informed about the disease due to proactive clinicians educating their patient bases, a greater number of consumer advertising campaigns, and a growing body of research on, and more public information about the condition. Patients increasingly understand that, though their symptoms often improve with treatment, DED generally is not curable so long-term therapy and compliance with the doctor's recommendations are paramount for successful management.³

Within the therapeutic realm, research continues to confirm many of our beliefs that transformative relief of dry eye symptoms comes systematically through a combination of lubricants, lid hygiene and ocular nutraceuticals, rather than a singular or isolated strategy. Expert guidance from the 2014 Dry Eye Summit⁴ suggests that clinical best practices for man-

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SYSTEMATIC APPROACH



Artificial Tears

+



Lid Hygiene

+



Oral Nutrition

aging all patients include this powerful triad, along with the addition of topical anti-inflammatories when necessary.

Looking more broadly at DED, a movement toward accurate classification of the disease has led to finely tuned definitions. In July, the Tear Film and Ocular Surface Society published the Dry Eye Workshop II (DEWS II)⁵ report, a follow-up to its 2007 predecessor, describing DED as “a multifactorial disease of the ocular surface characterized by a loss of homeostasis of the tear film...” This latest interpretation keenly accounts for the pivotal role that tear film hyperosmolarity and ocular surface inflammation play in the disease.

DEWS II, a nearly 400-page, evidence-based document involving 150 experts from around the world, unpacks the underlying

pathophysiology of dry eye and its central mechanism of evaporative water loss leading to hyperosmolar tissue damage.⁵ It describes how DED, either directly or by inducing a cascade of inflammatory events, contributes to a loss of epithelial and goblet cells that in turn decreases surface wettability, promotes early tear film breakup and further amplifies hyperosmolarity in an unforgiving spiral known as the “Vicious Circle.”⁵

Beyond the physical toll of DED, the report underlines the unseen human cost of uncontrolled dry eye.⁵ It exposes the possible adverse psychological impacts to the patient resulting from ongoing pain and blurred vision that may restrict the individual’s core activities and pleasurable pursuits, fostering a diminished social experience

and curbed enjoyment of life.⁵ Moreover, DEWS II quantifies the economic impact of DED in the United States, cited to be a staggering \$3.84 billion due to increased medical care spending, lost productivity and degraded quality of life.⁵

This latest and thoroughly vetted appraisal of dry eye and its profoundly invasive nature, as well as expanding knowledge about DED’s features, its response to various therapies and management plans, and the trajectory it likely will take is helping eye care professionals secure the right tools to thwart the forward momentum of dry eye. Clinicians are better poised than ever to offer greater comfort and peace of mind to patients suffering from the chronic burden of this disease.

— Terrence P. O’Brien, MD

Patient Presentation & Diagnosis

Dr. O’Brien: Do most patients present to your clinic with both signs and symptoms of dry eye?

Dr. McDonald: Most patients who come to our dry eye center of excellence have symptoms, but we do see a fair number of individuals with signs but no symptoms, and occasionally with symptoms but no obvious signs at the slit lamp, albeit with an elevated tear osmolarity and/or gland pathology seen on meibography.

Dr. Karpecki: Because I have a referral or advanced OSD clinic, my patients typically present with Sjögren’s syndrome, GVH or advanced evaporative dry



DEWS II & The Tear Film’s Central Role

In July, the Tear Film and Ocular Surface Society published the Dry Eye Workshop II (DEWS II)⁵ report with the following definition of dry eye, based on peer-reviewed evidence:

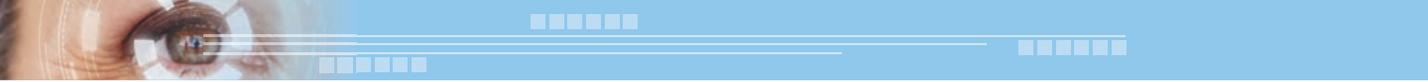
“Dry eye is a multifactorial disease of the ocular surface characterized by a loss of homeostasis of the tear film, and accompanied by ocular symptoms, in which tear film instability and hyperosmolarity, ocular surface inflammation and damage, and neurosensory abnormalities play etiological roles.”

The report says inclusion of the novel phrase “loss of homeostasis” helps clarify that tear film hyperosmolarity and ocular surface inflammation, along with neurosensory abnormalities, have causal etiologic roles and contribute to the common mismatch between signs and symptoms.

eye with significant atrophy of their meibomian glands. In this unique setting, about 90% have signs and symptoms. The remaining 10% have conditions like neuropathic pain and conditions that mimic, but are not,

dry eye.

Dr. Mastrota: When a patient has dry eye symptoms, I can usually isolate one clinical sign or risk factor to account for the patient’s symptoms. Some of the more subtle clues that I search



Obvious scleral show in a patient with complaints that are consistent with dry eye. Note the position of the lower eyelids, which generally are positioned tangential to the inferior limbus. Photo: Katherine M. Mastrota, OD, FAAO, Dipl. ABO

for are scleral show, conjunctival concretions and conjunctivochalasis.

Dr. Brujic: Dry eye, like many of the clinical conditions we treat on a daily basis, is often not straightforward. Sometimes patients have signs and symptoms, other times they will just have one or the other. The obvious symptoms include burning, itchy, dry and tired eyes, to name a few. But, given the potential visual impacts resulting from a dysfunctional tear film, it's important to always question patients about their vision, in particular visual instability.

Dr. O'Brien: The notorious discrepancy between symptoms and signs has made dry eye disease historically difficult to detect, study and treat. Symptom-free does not necessarily mean dry eye free, as nerve damage, systemic conditions

and environmental factors can contribute to asymptomatic dry eye. Clinicians need to fine-tune their antennas to hear the somewhat subtle complaints from patients of fluctuating vision, heightened intolerance to contact lens wear and increased blinking to see clearly, as clues of asymptomatic dry eye disease.

Dr. O'Brien: *Is there one tool that you use to diagnose dry eye, or do you have a set of tools that you use systematically together to determine dry eye status?*

Dr. Brujic: Unfortunately, one test cannot appropriately diagnose dry eye. A thorough slit-lamp evaluation can help determine the underlying cause of the condition. This includes: examining the eyelashes for madarosis, misdirected lashes and debris; inspecting the lid margin for integrity of the line of Marx; getting a closer look at meibomian gland orifices for signs of capping, visible inflammation and tylosis; evaluating eyelid elasticity and transillumination to gauge meibomian gland structure and the blink; investigating the conjunctiva for signs of hyperemia, chemosis and any redundancy; applying fluorescein and lissamine green to stain the corneal and conjunctiva to check for signs of lid wiper epitheliopathy; and measuring tear film break-up time.

Dr. McDonald: I also turn to a group of tools that includes a good history and a slit-lamp exam along with fluorescein and lissamine staining, tear osmolar-

Best Practices in Patient Management

Dr. O'Brien: *The 2014 Dry Eye Summit put forth basic management recommendations for dry eye disease that include the following protocol for all patients: ocular lubrication, lid hygiene and nutriceuticals.⁴ Do you agree with these recommendations for patients?*

Dr. Karpecki: I absolutely agree with the Summit protocol if you are managing patients with early or episodic DED, and feel more clinicians should be using it in this patient population.

Dr. Brujic: Lubrication is a sensible way to support the ocular surface. This palliative technique for symptoms relief can rehabilitate some of the eye structures, such as the cornea and conjunctiva, which may have suffered the sequelae of dry eye. However, artificial tears alone might not promote healthier tears. In order to truly foster an ocular surface that is producing suitable tears, elevating lid hygiene and optimizing tear production through nutritional and other means can offer added support, as the Summit's recommendations recognize.

Dr. O'Brien: Similarly, the Ngo et al. study⁶ showed improvement in dry eye signs and symptoms with the use of a combination of TheraTears[®] Lubricant Eye Drops, TheraTears[®] SteriLid[®] Eyelid Cleanser and TheraTears[®] Nutrition compared with subjects' habitual treatments. I believe all three of these components should be part of every patient's dry eye management strategy.

ity, meibography and MMP-9 testing.

Dr. Mastrota: I use multiple diagnostic methods as well—starting with an evaluation of the conjunctival integrity, and continuing with visual inspection, vital dye pooling and staining. Assessing the volume and uniformity of the lacrimal lake, and incorporating osmolarity and MMP-9 testing is of value, too.

Dr. Karpecki: Along the same lines, in addition to osmolarity testing and a validated questionnaire, I include meibomian

Dry Eye and Glaucoma: Shared Characteristics

Dry eye disease and glaucoma, though fundamentally different diseases, exhibit several common features such as they both:

- Are chronic, progressive conditions with an age-related increase in prevalence
- Require diligent medication compliance from patients
- Can be confounded by disparate subjective and objective findings
- Are unlikely to ever be "cured," relegating patients to a lifelong management regimen and some diminution of quality of life

O'Dell L. Glaucoma and dry eye: Principles and parallels. RCCL. 2015 Jan;27-31.

Dr. Brujic: Yes. This strategy makes so much sense. Clinically, it is promoting healthier tear production through boosting nutrition, minimizing excessive bacterial colonization with daily eyelid hygiene and providing a conducive environment for rehabilitation through use of artificial tears. There is no question that this method of managing dry eye is truly beneficial to improving patient outcomes.

Dr. O'Brien: With regard to omega-3 fatty acids specifically, although some clinicians have not embraced these essential polyunsaturated fats, their well-documented anti-inflammatory benefits are likely responsible for our consistently observed improvements in tear film stability and ocular surface staining in DED, especially among patients with MGD. As such, I recommend the dietary supplement of omega-3 EFAs as a first-line therapy. One important note about nutraceutical support: With the number of products on the market, patients can easily become confused when trying to select a source and quantity of omega-3 EFAs to supplement. Concerns about mercuric poisoning or other contaminants can further cloud their decision-making. So having a commercially available, high-grade source of omega-3s (ALA, DHA, EPA) in efficacious amounts and balance in a recognized formulation such as TheraTears® Eye Nutrition makes its inclusion a simple choice for my patients.

gland expression, dye staining, blink analysis as well as a thorough slit-lamp exam. And I do a cover test if structural and functional testing is normal. I've been amazed at how many patients have symptoms that mimic dry eye but have normal osmolarity, and it turns out the issue is eye misalignment such as convergence insufficiency. Osmolarity offers important clues about functional changes to the tearfilm, and meibography provides structural information. But as good as new technologies like point-of-care testing are, there

is still no one tool alone I would rely on for a dry eye diagnosis.

Dr. O'Brien: It's true that, though we have witnessed advancements in clinical detection of dry eye, no single, universal and unequivocal test exists to confirm disease. Similar to the other members of the panel, I use several approaches to classify the disease, assess severity and tear volume, determine progression and guide management.

Multiple Lines of Defense

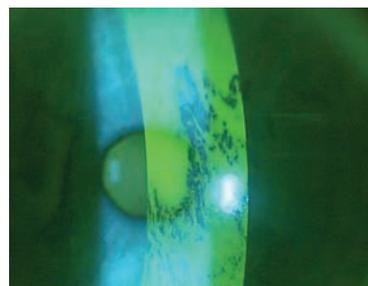
Dr. O'Brien: How do you customize treatment based on patient presentation? Do you have a treatment protocol for all newly diagnosed dry eye patients?

Dr. Karpecki: For more than 80% of my patients, there is an evaporative dry eye component. In these cases, I treat the obstruction, inflammation, biofilm and tear film components at once and adjust the therapy according to the severity of presentation.

Dr. McDonald: Over the years, I developed my own treatment algorithm for OSD using insights from the International Dry Eye (DEWS)⁷ and Meibomian Gland Dysfunction (MGD) workshops⁸ as a framework. My method includes, among other things, artificial tears QID and omega-3 nutritional supplements for mild dry eye patients.

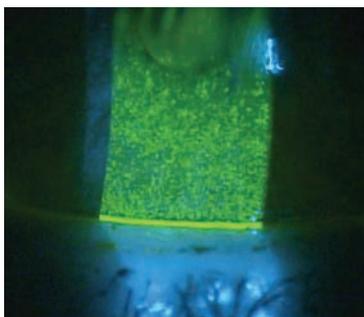
Dr. Brujic: An accurate assessment is key to selecting the most appropriate therapy. For example, a patient who complains of dry, itchy eyes and has significant blepharitis would be best-suited to a plan that involves sustained eyelid hygiene.

Dr. Mastrota: First, I gather information on any dry eye therapies the patient may be using or previously used, and ask for a detailed allergy history to see if other issues are at play. I establish quality lubricating eye drops



A patient displaying significantly reduced tear film break-up time. This photo was taken two seconds after the patient blinked.

Photos: Mile Brujic, OD, FAAO



Significant corneal staining in a patient with more severe dry eye.

in new ocular surface disease cases and as an adjunct for patients using other treatments. As a general rule, I add one therapy at a time to help me pinpoint which approach is helpful and which has less benefits.

Dr. O'Brien: Recent work on the ocular microbiome suggests that patients may be colonized with organisms yielding bacterial lipases that mediate the enzymatic cleavage of meibum

DEWS II Management Guidance: Restore the Tear Film

The DEWS II report published in July summarizes the following points about dry eye management and therapy:⁴

- In the management of DED, restoration of tear film homeostasis is the ultimate goal, which involves “breaking the vicious circle of the disease”
- A major challenge in DED management is to develop management and treatment strategies that are not overly complicated for patients



into free fatty acids and soaps—possibly contributing to ocular irritative symptoms and an unstable tear film. Use of an effective lid cleansing agent with antimicrobial and anti-inflammatory properties such as TheraTears® SteriLid® Eyelid Cleanser is my first-line therapy to reduce excessive colonization, stabilize the tear film and improve evaporative dry eye.

I FEEL THAT THE TRIAD OF TEARS, HYGIENE AND OMEGAS ARE SIMPLE AND BASIC STRATEGIES FOR OCULAR SURFACE DISEASE MANAGEMENT.

- Dr. Mastrotta

Dr. O'Brien: Do you typically rely on one primary treatment for dry eye patients, or do you recommend multiple therapies as part of a systematic approach?

Dr. McDonald: I have two fairly involved treatment algorithms, one based on osmolarity, and the other on lid disease analysis. Since patients frequently have dry eye and MGD concomitantly (86 to 92% of the time⁹), I usually advocate a plan that incorporates aspects of both algorithms.

Dr. Mastrotta: I rely on multiple approaches. Initially, I discuss lid hygiene with my patients and ask about their use of lid cleaning products, including eye makeup remover and daily face cleaners. In addition, increasing scientific evidence supports the incorporation of omega fatty acids for DED, so I am comfortable with recommending omegas in my management of dry eye for most patients. I feel that the triad of tears, hygiene and omegas are simple and basic strategies for ocular surface disease management. Tears rinse

away allergens and support the ocular surface by reducing shear stress. Hygiene addresses bacterial skin and fungal loads, environmental debris and irritants in makeup, as well as aerosolized products such as cleaners and skin contaminants. Omegas contribute an anti-inflammatory component, which is important considering that inflammation is thought by many experts to be the overarching concern with dry eye disease.

Dr. Brujic: I also turn to a multifaceted approach and augment it with mechanical eyelid treatment (e.g., eyelid debridement) in addition to chemical modification to the way the patient's tears are being produced.

Dr. Karpecki: Likewise, I depend on multiple therapies to allay symptoms.

Dr. O'Brien: I feel that a non-specific, "shotgun" approach to management should be avoided. The complex, multifactorial pathogenesis involved in DED typically necessitates a systematized, multimodal and rational treatment approach to ameliorate symptoms, reverse signs and reestablish homeostasis of the ocular surface.

Augmenting the Protocol With Other Therapies

Dr. O'Brien: Do you always recommend an OTC artificial tear before turning to a prescription medication? When do you turn to a prescription medication?

Dr. Mastrotta: I generally start therapy with an artificial tear and increased water intake. If my patient is using tears four times a day or more without relief, especially if they are under 40 years old, then I will add a prescription medication. I often will continue lubrication QID with other Rx medications.

Dr. Brujic: Artificial tears are an indispensable supplement to any dry eye patient's regimen.

They provide comfort and help restore the health of the ocular surface. Unless dryness is sporadic, the treatment regimen should also include something beyond an artificial tear. That is assuming the eyelid margin is not overpopulated with bacteria or *Demodex* and that pharmaceutical management is appropriate to assist with tear production.

Dr. O'Brien: Since dry eye can result in permanent alterations to the ocular surface over time, early intervention is important to halt progression. It's important to remember that severe disease starts out as mild disease, so artificial tear supplementation to reverse osmolar perturbations along with prescription anti-inflammatory medication to control inflammation should be considered for patients with mild to moderately severe DED.

Dr. Karpecki: I rarely recommend OTC artificial tears since most of my patients have already tried them before seeing me for DED. However, I do switch the patient to the best available artificial tears along with prescription medications at the beginning.

Dr. O'Brien: Is there value in using OTC artificial tears in conjunction with Rx products?

Dr. Karpecki: Absolutely—to increase comfort until the patient starts producing quality tears, which can take six to 12 months and may not fully occur in all patients. There will also be flare-ups or situations in which artificial tears, such as TheraTears® Dry Eye Therapy™ lubricant eye drops, will be beneficial, even after inflammation, biofilm and obstruction are controlled. And hypotonic artificial tears can help lower elevated tear film osmolarity, regardless of the type of dry eye, which is key to getting the tear film back to homeostasis.

Instituting a Systematic Treatment Strategy

Here are practical suggestions from the panel of experts to help eye care practitioners institute a systematic dry eye management approach:

- **Make it a priority to educate patients and the staff at every turn.** Hold frequent team meetings, however brief, to discuss patient education strategies and recognize staff members for doing a good job of increasing patient awareness.
- **Create a standardized diagnostic protocol in the office that incorporates one test you currently are not doing.** After that becomes a habit, add one more, and continue doing this. For treatment, consider supporting the ocular surface with mechanical and pharmacological means, and the use of artificial tears.
- **Standardize DED detection and management to achieve positive results.** In addition, celebrate progress with patients, and recognize the need for aggressive approaches in more severe, less responsive cases to improve patient outcomes and satisfaction.
- **Listen to your patients and know that you can positively impact their quality of life.** Remember that there is always one more question you can ask your patients that may help you construct the most impactful therapy for them.

Dr. McDonald: Agreed. Though Rx products are effective for moderate to severe dry eye, most patients still need additional support from palliative therapies such as OTC tears, especially individuals working in environments that pose a challenge to dry eye (e.g., long hours in front of the computer, an office with forced air heating and cooling, etc.).

Dr. Brujic: I also see a great deal of value in augmenting an Rx with artificial tears, in particular when the ocular surface is initially in repair mode. Ultimately, the goal is to rehabilitate the ocular surface in order to produce tears in a more efficient manner.

Dr. O'Brien: I endorse the benefits of this strategy as well. One role of tear hyperosmolarity in response to desiccation stress is to activate intracellular signaling pathways and trigger the release of proinflammatory cytokines, priming the local immune system. Chemical mediators released by activated T-cell lymphocytes in this cascade perpetuate the inflammatory pathway on the ocular surface. So replenishing the tear film with lubricants that reduce hyperosmolarity and relieve desiccation stress is fundamental to overall

therapeutic success.

Benefits Reaped From a Systematic Approach

Dr. O'Brien: *What evidence do you have that a systematic approach to dry eye treatment/management is helping your patients?*

Dr. McDonald: For one thing, our patients' symptoms improve. Secondly, we observe

HYPOTONIC ARTIFICIAL TEARS CAN HELP LOWER ELEVATED TEAR FILM OSMOLARITY, REGARDLESS OF THE TYPE OF DRY EYE, WHICH IS KEY TO GETTING THE TEAR FILM BACK TO HOMEOSTASIS.

- Dr. Karpecki

marked changes to some or all of the following benchmarks: tear osmolarity scores decrease, MMP-9 tests become negative and meibomian gland loss is halted.

Dr. O'Brien: Our success is evident by improved validated questionnaires of ocular symptoms, prolonged tear break-up time, as well as increased tear volume/production, normaliza-

tion of tear-film osmolarity and resolution of inflammation, seen on MMP-9 testing.

Dr. Brujic: We know beneficial progress is happening based on what patients are telling us and also by our clinical findings.

Both types of feedback are critical to determining whether success or failure is being achieved with any treatment regimen.

Dr. Karpecki: Similar to the Ngo et al. study results revealing significant improvements in patient symptoms, eyelid margin features, and meibomian gland features and function using a systematic method to address DED, our internal data reveal that about 97% of our patients are satisfied or very satisfied with the systematic treatment plan we put forth for their dry eye disease. They are amazed at the favorable therapy responses occurring in their eyes after decades of no change.

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