

THE PYRAMIDS OF DRY EYE DISEASE: A SIMPLIFIED MODEL TO GUIDE DED MANAGEMENT

Relying on evidence-based medicine could be key to establishing an algorithm to manage dry eye disease effectively.

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Our clinician colleagues in oncology have discovered that there is no single cancer, let alone a single cure for cancer. Ocular surface disease is certainly not cancer, but it manifests from similarly multifactorial sources. Some patients may present with meibomian gland dysfunction. Others may present with evaporative dry eye disease (DED). Still others may present with eyelid issues. Our job is to determine which is which and then to apply appropriate management strategies.

Determining the source of DED requires careful examination, a critical mind, and a recipe for success. Below, medical student Tanner Ferguson, BS, joins forces with Drs. Ferguson, Hansen, and Blackie to describe an algorithm for DED that others may find useful. It should be stressed that their algorithm—while based in science—has not been vetted in a clinical trial but is utilized by Dr. Ferguson in his own clinical practice. Still, the authors' reliance on peer-reviewed data and protocols should push us all toward relying on evidence as the model for algorithm genesis and adjustment.

—Andrew S. Morgenstern, OD

Dry eye disease (DED) is the progressive, chronic medical eye diagnosis ophthalmologists and optometrists most frequently encounter: Estimates of the percentage of people worldwide with DED range from 5% to 34%.¹⁻³ Since 2007, clinical research has relied on evidence-based science to understand and improve clinical care by using algorithm-based and targeted approaches to DED management,⁴⁻⁶ and working groups have established guidelines for classification of DED severity, leading to targeted treatment.⁷ Still, clinicians are confronted with a plethora of treatment options for DED management. Treatment of DED continues to feel like trying to hit a bullseye without knowing the location of the target.

EVIDENCE-BASED PRACTICE

The quest for one gold standard treatment option that will treat all DED cases efficiently and effectively is doomed to fail because not all patients present with the same condition. That is, the combination of symptoms, visual disturbances, ocular surface damage, tear film instability, increased osmolarity, and inflammation at the root of DED varies from patient to patient.

Therefore, clinicians should approach each patient with an evidence-based foundation focused on stabilizing all of DED's contributing factors. The pyramid approach to DED management we present in this article aims to provide a consistent process for treatment and long-term care of DED



The dry eye algorithm presented here can help patients understand the long-term nature of their disease and guide clinicians toward evidence-based solutions.

patients. Literature reviews and teaching models have generally failed to look at all possible contributing etiologies as an initial management strategy and do not measure the contributions of every possible factor in DED care in a concise, clinically based format. The pyramid diagram for comprehensive DED management (Figure) effectively demonstrates the complexity of the syndrome in a concise model that captures DED's diagnosis, treatment, and chronicity.

Outcomes will vary based on patient compliance, and it should be noted that compliance generally improves when adequate education is provided about all the factors that may influence the tear film. The desired result is ocular surface homeostasis, with the intent to provide opportunity for long-term stability.

PYRAMIDS

Our algorithm relies on three pyramids—green, yellow, and red—which represent three important clinical phases in the pathogenesis and management of DED (Figure). The large green pyramid represents initial diagnosis and treatment designed to reconstruct the tear film, optimized by the patient's own physiology, with the goal of a homeostatic ocular surface. The base of this pyramid shows the foundations of DED management, the issues that every DED patient must address with his or her clinician. The yellow pyramid represents adjunctive therapy that must be deployed to keep the tear film stabilized following initial therapies to reach peak homeostasis. The red pyramid, inverted to illustrate the chronic nature of the disease, represents the future in which treatment will likely have to be revisited.

In addition to being a helpful guide to clinicians, these pyramids are a visual tool that can help patients to comprehend the nature of the disease and the complexity involved in trying to stabilize their disease. The pyramids of tear film reconstruction and ocular surface rehabilitation provide excellent models for students and clinicians attempting to comprehend and manage the complexity of DED. In particular, the inverted red pyramid helps to drive home the point to some patients that this disease may “turn upside down” on them and will require reassessment and retreatment.

FOUNDATIONS

The foundations at the base of the green pyramid represent what the authors believe are the critical clinical groupings that must be addressed in every ocular surface disease patient, as both causes and masquerades of DED.

Lid Anatomy, Physiology, and Function

The eyelid must be anatomically correct in order to perform its primary functions of protecting and wiping tears across the ocular surface. The quality and blink rate of the lids are paramount for tear film optimization. Meibomian gland function is pivotal to tear film composition.

Allergies

Often overlooked, allergies can complicate and masquerade as DED. A plan must be in place to control the inflammatory consequences of allergies on the physiology of tear film composition when applicable.

Lid Margin Disease

Often the first stage in the sequential ocular surface disease process, lid margin disease requires separate consideration in all patients.

Diet

Counseling patients on nutrition is extremely important. Poor nutrition can lead to oxidative stress and inflammation, leading in turn to unhealthy tears.^{8,9}

Medications

Some medications cause physiologic changes to the tear film composition that can masquerade as DED symptoms through the influence of the trigeminal nerve and the autonomic nervous system.

Systemic Disease

Refractory ocular surface disease is often influenced by underlying systemic disease. The best tear film treatment and reconstruction can be weakened by the impact of the body's overall physiologic stability.

Referred DED

Recently, investigators have described symptoms of DED that may occur when disruption of normal binocular function is not addressed.¹⁰

It is often stated that contact lenses, laser vision correction, or environmental conditions can cause DED.¹¹⁻¹³ However, it may be more accurate to say that these factors may exacerbate an already subclinical problem. Not all patients who wear contact lens, are exposed to arid conditions, or have laser vision correction develop DED. Contact lenses, laser vision correction, and environmental conditions should be viewed as associated factors, more likely to be of importance in the patient with a fragile and unstable tear film.

GREEN PYRAMID: STABILIZING THE TEAR FILM

The green pyramid in our scheme contains three steps: diagnosis, tear film reconstruction, and maintenance of homeostasis.

Diagnostic Workup

Managing the signs and symptoms of DED and addressing its underlying causes in a particular patient can be accomplished only if the clinical workup of that patient includes a comprehensive assessment of all the elements required to construct and maintain an optimized tear film. Modern

COMPARING EYE CARE TO DENTISTRY

Experts in DED understand the multifactorial nature of the disease but still struggle to effectively communicate the nature of the disease to patients.¹ Many experts have underemphasized the role of chronic exposure in evaporative stress, which directly affects long-term maintenance and disease management and the etiology of the condition itself. Awareness of and control of evaporative stress is every bit as critical to the long-term treatment of DED as rehabilitating the tear film and ocular surface.

Some patients may struggle to grasp the implications of evaporative stress on long-term DED management. When an eye care provider senses that a patient does not grasp the importance of evaporative stress, it may be useful to rely on

anatomic analogies to which the patient can relate. We frequently compare the ocular surface to the dental surface and compare tear film dysfunction to dental plaque accumulation that leads to gum disease.

Patients understand that dental plaque cannot simply be rinsed away or controlled with medication and that they must embrace lifestyle adjustments and daily care to keep it in check. It is not a far jump to see that the ocular surface requires the same maintenance and that similar lifestyle adjustments may be required.

1. Baudouin C, Aragona P, van Setten G, et al; ODISEY European Consensus Group members. Diagnosing the severity of dry eye: a clear and practical algorithm. *Br J Ophthalmol*. 2014;98(9):1168-1176.

technology enables clinicians to perform an efficient and comprehensive assessment so that the building blocks of therapy can effectively be applied to each patient.

Patient questionnaires present a subjective format to allow patients to assess their symptoms. Diagnostic tests aid in diagnosis and treatment by providing visual and quantifiable data. In our practice, we utilize LipiScan and LipiView (Johnson & Johnson Vision) for meibomian gland imaging, the Keratograph (Oculus) for corneal topography, tear osmolarity testing (TearLab), and InflammDry (Quidel) testing for inflammatory markers.

Despite these advanced technologies, physical examination of the ocular surface with dyes such as fluorescein remains the most critical step for evaluating etiology and staging the level of severity.

Tear Film Reconstruction

Historically, treatment of DED has focused on aqueous-deficient management strategies and tear film stimulation.¹⁴ The clinical focus was on reducing inflammation, quieting symptoms, and, ultimately, delivering relief to the patient.

Given the multifactorial and heterogeneous nature of DED, many patients require varied combinations of therapy to restore their tear film. For example, a patient with meibomian gland dysfunction (MGD) may have significant ocular surface inflammation, lid margin disease, and abnormal blink pattern. For such a patient, we may recommend therapies such as thermal pulsation treatment, adjunctive short-term steroid use, nutritional supplementation, lid margin disease treatment, and blink exercises. The ultimate goal is an optimized tear film with ocular surface stability.

Systemic Disease Stabilization

Disruption of the systemic physiology can adversely affect direct treatments of the tear film and ocular surface health. Collaboration with other medical specialists may be necessary to optimize treatment plans through systemic disease management.

Ocular Surface Inflammation Control

Amniotic tissue grafts, steroids, NSAIDs, cyclosporine ophthalmic emulsion 0.05% (Restasis, Allergan), and lifitegrast ophthalmic solution 5% (Xiidra, Shire) are all part of the armamentarium of options to treat inflammation. Severity of disease state, chronicity, and other foundational factors guide their use in DED and ocular surface disease treatment.

Meibomian Gland Function Optimization

The only treatment approved by the US Food and Drug Administration for meibomian gland dysfunction is vectored thermal pulsation (LipiFlow, Johnson & Johnson Vision). This treatment is foundational to successful outcomes in most patients with ocular surface disease.¹⁵

Tear Volume Optimization: Retention and Stimulation

Punctal plugs, punctal cautery, and medications to stimulate tear production (such as cyclosporine and lifitegrast) aid in the reconstruction of the aqueous-deficient tear film.

Lid Margin Disease Treatment

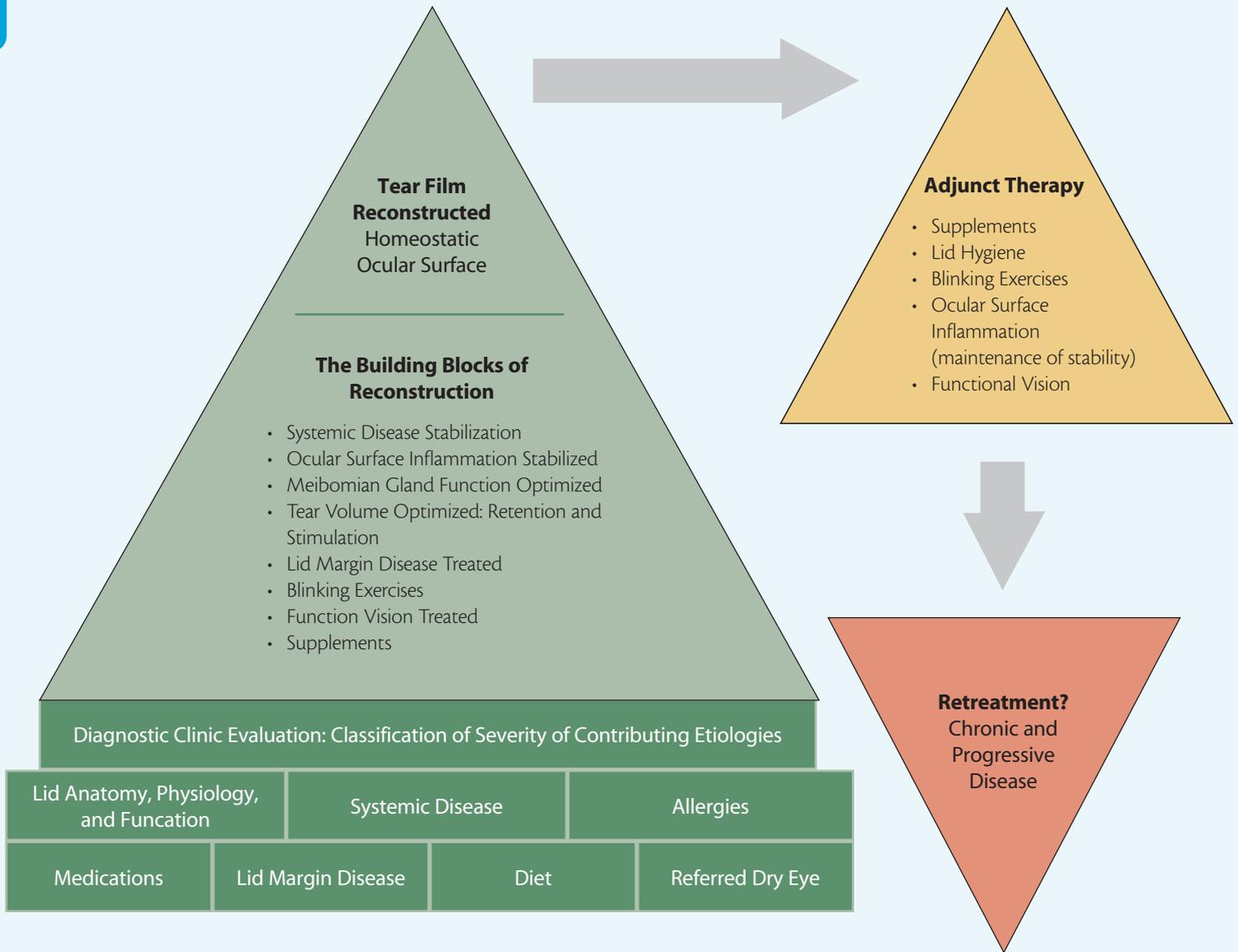
Fundamental treatment in almost all cases with eyelid cleansers such as Avenova (NovaBay) and Cliradex (Cliradex) and electromechanical lid margin debridement (BlephEx, Rysurg) have replaced traditional warm compress or diluted baby shampoo.

Blinking Exercises

Blinking exercises in the digital world can be an important adjunct to MGD treatment to keep glands activated and expressing meibum. The mobile app Donald Korb Blink Training can be a good way to help patients stay on top of their blinking exercises.

Functional Vision Treatment

Emerging science and technology utilizing progressive prism lenses has provided relief for neuropathic referred DED (nonphysiologic DED complaints) in Dr. Ferguson's clinical



The Foundations of Dry Eye Disease Management

Figure. A three-pyramid structure for evidence-based and long-term DED management.

practice. However, to the best of our knowledge, there are no published studies available to support this yet.

Supplements

Nutritional supplements containing omega-3 fatty acids, such as HydroEyes (ScienceBased Health), have been demonstrated to be effective in symptom relief in patients with DED.^{16,17}

YELLOW PYRAMID: ADJUNCTIVE THERAPY

Ocular Surface Homeostasis

The recently revised definition of DED promulgated by the Dry Eye Workshop II now recognizes the centrality of “loss of homeostasis of the tear film” in DED.⁶ Effective management of DED therefore requires us to concentrate on restoring and maintaining that homeostasis. Several adjunctive therapies can help our patients to achieve this.

Maintenance of Stability

After ocular surface hemostasis has been achieved via foundational tear film reconstruction, the next step is maintenance of stability. Chronic disease states require consistent (and often multiple) adjunctive therapies. Lid margin hygiene, dietary supplementation, blinking exercises, and low grade antiinflammatory drops may all be needed to support the ocular surface.¹⁸

RED PYRAMID: RETREATMENT

DED and subsequent ocular surface disease are chronic in nature and can often recur despite therapy that addresses the initial etiology. The fundamental goal of therapy is to stabilize the condition and to maintain homeostasis of the ocular surface. The potential that we will have to repeat reconstruction and rehabilitation of the tear film remains for each patient, despite an initially effective treatment plan.

Treatment in most cases is not a cure but a retardation of progression. The red pyramid serves as a warning that disease may recur regardless of treatment or because of poor patient compliance. This pyramid encourages patient compliance, as patients do not want to be placed in the inverted pyramid group and have to start from scratch.

EXPANDING VISION OF DED

Recent DED research challenges the practicing eye care provider to integrate evidence-based care into his or her practice. The days when only one factor was considered in DED are over. The triple pyramid approach outlined in this article provides today’s DED expert the ability to implement a consistent and systematic process in patient care and distills a complex disease process with an orderly construction process that is patient-centered to help guide clinicians.

Armed with modern technology and numerous evidence-based treatment options, we can effectively treat DED patients with increased predictability and confidence. These advantages will be realized only if we use evidence-based algorithms in our approach as clinicians and educators. ■

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