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THE VALUE OF REAL TEARS

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The ocular surface is constantly undergoing desiccating stress but, under normal circumstances, is protected from damage by the production of a stable, homeostatic tear film.[1] Therefore, restoring tear film homeostasis is a major goal of dry eye management, and the patient's ability to produce real tears of sufficient quality and quantity should be taken into account when starting dry eye treatment.[2,3]

Tear film instability is a central driver of the complex cascade leading to clinical signs and symptoms of dry eye disease.

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One of the reasons that a stable tear film is important is because it accounts for the majority of the refractive power of the eye, with tear film instability leading to reduced contrast sensitivity and increased optical aberrations.[3] A stable tear film also provides lubrication, protection, and nourishment to maintain a healthy ocular surface and has been a noticeable feature of many definitions of dry eye throughout the years (**Figure 1**).[4-7]

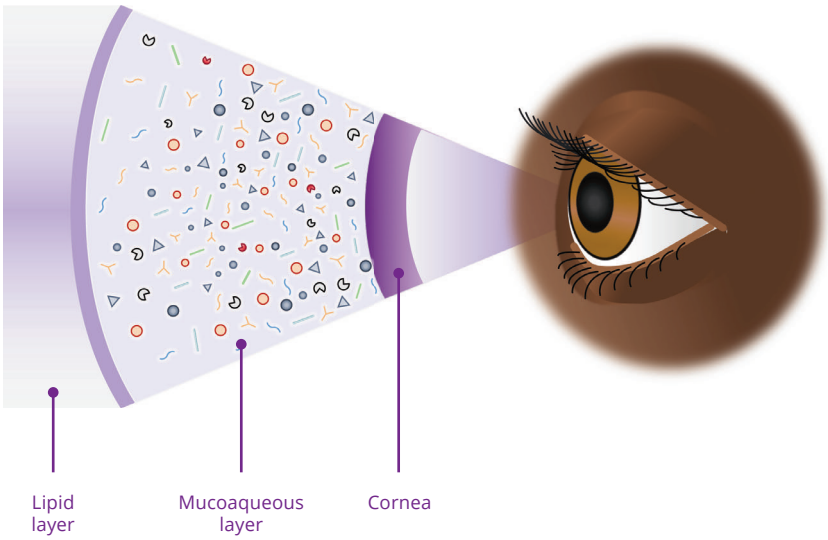

FIGURE 1:
A stable tear film accounts for the majority of the refractive power to the eye and the compounds found in the tear film provide lubrication, protection, and nourishment to the ocular surface.[3,4]

Almost all the definitions that have been proposed for dry eye, including those promulgated by TFOS DEWS II (2017) and the Global Consensus group (2020), have highlighted the idea that dry eye progression is driven by a cycle of tear film instability, hyperosmolarity, ocular surface damage, and inflammation.[7,8] Tear film stability can be compromised by decreased tear secretion, delayed tear clearance, and/or altered tear composition, which starts the cycle of dry eye and subsequently leads to the loss of homeostasis and ocular surface inflammation.[1,9,10]

GLOBAL CONSENSUS DEFINITION (2020)

"Dry eye is a multifactorial disease characterized by a persistently unstable and/or deficient tear film causing discomfort and/or visual impairment, accompanied by variable degrees of ocular surface epitheliopathy, inflammation, and neurosensory abnormalities."[7]

"

An unstable tear film is a critical initial step causing the downward spiral of the ocular surface leading to dry eye, tissue damage, and inflammation.

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Tears are a complex mixture of elements and can come in four different types (basal, reflex, emotional, and closed-eye), each of which has a slightly different composition and function.[4-6,11,12] Basal tears are those that are present during the waking hours and are constantly being turned over. They are considered the primary tear that helps to maintain a healthy, functional ocular surface. Physical stimuli (eg, foreign bodies, trauma) to the eye produce a larger volume tear which is termed a reflex tear. Similarly, emotional stimuli (eg, sadness) also produce a larger volume tear called an emotional tear. The final tear type is the closed-eye tear that is produced when the eye is closed during a sleep cycle.[11,12]

Real tears, including basal tears, contain a complex milieu of over 2000 different components, each of which contributes to tear film stability and function (**Figure 2**). Among the many different components found in the tear film are proteins that protect the ocular surface and help it function (eg, growth factors, anti-inflammatory proteins), electrolytes and metabolites that play a role in basic cell metabolism, and mucins and lipids that help maintain tear film stability.[4-6]

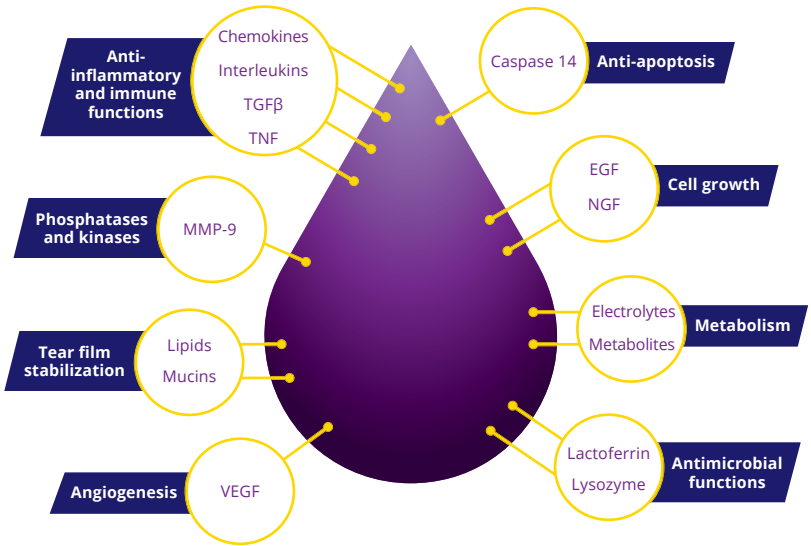

FIGURE 2:
Real tears, including basal tears, contain a complex milieu of over 2000 different components, each of which contribute to tear film stability and function.[4-6] This is just an example of some of the many components found in the tear film and their possible function.

With over 2000 components within a healthy human tear, treatment of dry eye should take into consideration the production of healthy, real tears.

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The tear film and its many components are created and cleared by the lacrimal functional unit (LFU), which consists of the main and accessory lacrimal glands, meibomian glands, conjunctival goblet cells, and the lacrimal drainage system that is interconnected by sensory and motor nerves. The nerves of the LFU connect it to the central nervous system (CNS) via the trigeminal nerve and the trigeminal ganglion. Stimuli from either the ocular surface or the nose are transduced through the trigeminal nerve to the CNS (the afferent pathway) and then transmitted via efferent pathways to the secretory tissues (eg, main and accessory lacrimal glands, conjunctival goblet cells, and meibomian glands) and muscles that drive tear production and blinking (**Figure 3**). Stimulation of the LFU from intrinsic and extrinsic factors regulates tear production and helps produce a homeostatic tear.[1,3] For instance, normal, unlabored breathing and consistent airflow through the nasal passageways provide constant sensory stimuli to the LFU, which accounts for approximately 34% of basal tear production.[13]

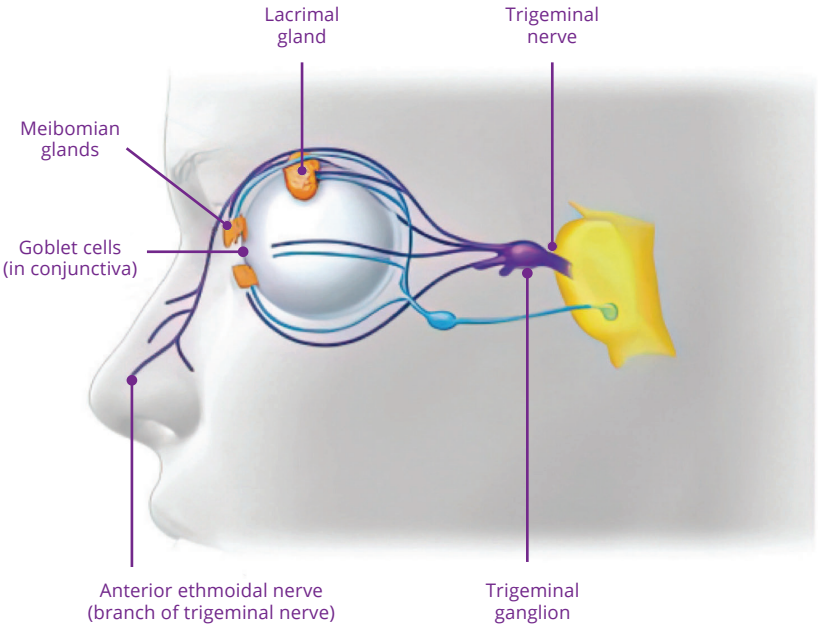

FIGURE 3:
Tears are created and cleared by the lacrimal functional unit (LFU), which consists of the main and accessory lacrimal glands, meibomian glands, conjunctival goblet cells, and the lacrimal drainage system that is interconnected by sensory and motor nerves. The nerves of the LFU connect it to the central nervous system via the trigeminal nerve and the trigeminal ganglion.[1,3] In this illustration, the afferent pathway is shown in purple, the efferent pathway is shown in blue.

It is widely acknowledged that dry eye is a multifactorial disease with many different etiologies. However, regardless of the etiology, the main goal of dry eye management is to break the cycle of dry eye by restoring tear film homeostasis, which can prevent the disease from either recurring or increasing in severity.[2,3] Dry eye treatment plans often start with environmental and behavioral modifications to reduce potential triggers and the implementation of lid hygiene regimens, as well as the use of artificial tears.[2] Artificial tears are considered a cornerstone of dry eye treatment and are formulated to mimic or supplement the mucoaqueous and lipid layers of the tear film.[2] However, they do not contain the biologically active components found in real tears and are temporary, palliative treatments that do not directly address the underlying etiology of dry eye.[2,14]

Furthermore, patients may encounter certain problems when using an eyedrop like an artificial tear. Depending on their age and dexterity, some patients may not be able to get a drop into their eyes or may have difficulties squeezing the bottle and others may dispense too many drops at a time.[15] Many patients initially choose to self-treat with artificial tears and may incorrectly use them.[16] Also, because each drop is a larger volume than that of the real tear film, they may induce reflex tearing and blinking and wash away natural components found in the tear film.[17]

Restoration of tear film homeostasis and disruption of the cycle of dry eye may be achieved by creating a real tear.

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Additionally, artificial tears may contain anti-microbial preservatives that have been shown to harm the ocular surface and further exacerbate the signs and symptoms of dry eye. Benzalkonium chloride (BAK) is one of the most common anti-microbial preservatives used in eye drops and evidence suggests that BAK adversely effects the ocular surface by being toxic to corneal and conjunctival cells, including conjunctival goblet cells and corneal nerves, and delaying corneal wound healing.[2,18]

If patients have tried artificial tears and continue to have dry eye signs or symptoms, they are likely to be switched to a prescription eye drop, either an anti-inflammatory or a lipid layer enhancer.[2] While these prescription drops have been shown to treat dry eye, they may also have their difficulties. For instance, these eye drops need to be administered either twice or four times a day and are not compatible with contact lenses; for each administration, the patient must remove their contact lenses and keep them out for up to 30 minutes after instilling the drop.[19-24] Other approaches such as devices (eg, intense pulsed light therapy), tea tree oil, punctal occlusion, or therapeutic contact lenses may be used depending on the type of dry eye present and its severity.[2]

Nasal neurostimulation provides an alternative approach for the treatment of dry eye as it does not require patients to instill eye drops. Since part of the LFU can be accessed via the nasal cavities, it can be stimulated to induce the lacrimal glands, meibomian glands, conjunctival goblet cells, and other components of the LFU to produce basal tears.[1-3] Unlike artificial tears that mimic specific components of the tear film, nasal neurostimulation is thought to induce the production of a real tear.[13]

If the goal of dry eye therapy is to break the cycle of dry eye, then one key mechanism to doing so may be to stimulate the creation of real tears and restore tear film stability.[1-3] While artificial tears are a step in the right direction, they offer temporary, symptomatic relief without addressing the underlying causes of dry eye.[2,14] The other common treatment option, anti-inflammatories, specifically targets inflammation, which is downstream of tear film stability and does not directly restore tear film homeostasis.[2,9] Therefore, treatment for dry eye should begin by adequately addressing tear film instability as a distinct process, thereby breaking the cycle of dry eye.

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