Growth Factor Supplementation: A New Paradigm in Ocular Surface Disease Management

Insights from Expert Clinicians | 🍐 Vital Tears



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Growth factors play a crucial role in maintaining ocular surface homeostasis and health and promoting healing in various ocular disorders.¹ As our understanding of these molecules evolves, so does their potential for therapeutic application. To explore the current state of knowledge and clinical practice regarding growth factors in ocular surface disease, Vital Tears recently convened a roundtable discussion with five internationally renowned clinicians specializing in dry eye and ocular surface disorders: **Clara Chan**, **Minas Coroneo, Pedram Hamrah, Victor L. Perez**, and **Stephen Pflugfelder**.

Currently, there are limited peer-reviewed publications and no consensus on the management of ocular surface disease using growth factor supplementation. The aim of this panel discussion was to delve into the basic science of growth factors, their specific roles in ocular surface health, and their applications in clinical practice.

Understanding Growth Factors and Their Role in Ocular Surface Health

Growth factors are a diverse family of naturally occurring molecules that stimulate cellular growth, proliferation, healing, and differentiation.² The ocular surface is home to a complex interplay of various growth factors, including epidermal growth factor (EGF), transforming growth factor-beta (TGF- β), nerve growth factor (NGF), fibroblast growth factors (FGFs), and vascular endothelial growth factor (VEGF), among others. These factors are found in natural tears and work in concert to maintain ocular surface homeostasis and to regulate repair of the corneal epithelium and other ocular surface structures.³

Dr. Minas Coroneo highlighted that the application of growth factors to the ocular surface was inspired by the early use of autologous serum-based eye drops in the 1930's and reprised their use in cell culture media, where fetal calf serum was found to promote cell growth.

This has led to the exploration of serum-derived products for ocular surface treatments. Dr. Clara Chan emphasized the diverse functional importance of growth factors in improving tear

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quality, regenerating nerve function, providing anti-inflammatory properties, and supporting limbal stem cells. She noted that growth factors can stimulate healing in various conditions, including ocular burns and epithelial breakdown.

Key Growth Factors and Their Effects on the Ocular Surface

Of the many growth factors present in tears and in serum, several can be highlighted for particular importance to the ocular surface.

Epidermal Growth Factor (EGF)

EGF is a well-studied growth factor that has significant implications for ocular surface health. According to Dr. Stephen Pflugfelder, EGF is secreted by the lacrimal glands, and possibly produced by epithelial cells on the ocular surface. EGF is present at high concentrations in human tears and plays a crucial role in corneal epithelial proliferation, differentiation, and migration, which makes it essential for wound repair.

Transforming Growth Factor-beta (TGF-β)

TGF-β is a multifunctional cytokine with complex and sometimes contradictory effects on the ocular surface. Dr. Pflugfelder emphasized that the effects of TGF-β are highly dependent on concentration, cell type, and context.

In the context of epithelial healing, TGF-β can inhibit epithelial proliferation. However, when working in tandem with other growth factors, such as EGF, FGF, or insulin-like growth factor, TGF- β may help coordinate the epithelial healing response.

Nerve Growth Factor (NGF)

In recent years, NGF has gained significant attention owing to its role in promoting corneal nerve health and healing. The FDA

Growth Factor	Role in Ocular Surface Health & Healing
Epidermal Growth Factor (EGF)	Plays a crucial role in corneal epithelial proliferation, differentiation, and migration.
Transforming Growth Factor-beta (TGF-β)	Works in tandem with other growth factors, to help coordinate the epithelial healing response. Also helps control inflammation on the ocular surface.
Nerve Growth Factor (NGF)	Promotes corneal nerve health and ocular surface homeostasis by supporting epithelial and neuronal health, limbal stem cell proliferation, immune modulation and production of a healthy tear.

approval of recombinant human nerve growth factor (cenegermin) for neurotrophic keratitis has provided an available treatment for NGF supplementation. However, Dr. Hamrah noted that some patients may require long-term maintenance therapy to achieve and sustain clinical improvement.

Benefits of Growth Factor Supplementation in Ocular **Surface Diseases**

Growth factor supplementation, particularly through autologous serum tears, holds potential for enhancing patient outcomes in ocular surface diseases.³ Administration of serum tears is the only currently available route that allows for supplementation of the tear film with multiple growth factors simultaneously, promoting ocular surface healing.

Dr. Hamrah explains to patients that serum growth factors are regenerative, helping to fix damaged nerves and epithelium and that the use of multiple growth factors, as found in serum, is more effective than using a single growth factor eyedrop. Autologous serum tears also contain numerous vitamins and lysozyme as well as EGF and TGF- β , in contrast to commercially available eyedrops that

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Dry Eye Disease

While the etiology of dry eye disease is multifactorial, growth factor supplementation may address a critical aspect of ocular surface dysfunction. Dr. Pflugfelder suggested that growth factors could be the "missing piece" in the dry eye treatment puzzle, potentially working in conjunction with other therapies to restore ocular surface homeostasis.

Serum tears provide a complex mixture of growth factors, vitamins, and other beneficial molecules that synergistically promote ocular surface health.

Dr. Chan emphasizes to patients with dry eye disease that their poor tear quality equates to inadequate nutritional support. She explains that the growth factors in serum tears help improve the tear quality, regenerate some of the nerve function on the surface of the eye, provide anti-inflammatory properties, and heal the punctate epithelial erosions on the corneal surface.

Neurotrophic Keratitis

Dr. Chan discussed the use of growth factor supplementation in patients with chronic neurotrophic disease, explaining that serum tears can provide the necessary growth factors to stimulate healing in patients with poor corneal sensation. She noted, however, that these patients rarely regain nerve

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Growth factor supplementation should be considered earlier in the treatment algorithm for dry eye disease. Even patients with milder forms of ocular surface disease may benefit from early growth factor supplementation to prevent disease progression.

function spontaneously and may benefit from long-term therapy.

Dr. Hamrah added that NGF therapy has shown promise not only in treating established neurotrophic ulcers but also in managing earlier stages of neurotrophic keratitis to prevent disease progression.

Neuropathic Corneal Pain Growth factor supplementation, particularly with NGF and other neurotrophic factors, has also shown promise in managing neuropathic corneal pain. Dr. Hamrah explained that the combination of growth factors and anti-inflammatory molecules in serum-derived products might help address both the nerve damage and inflammatory components of neuropathic pain.

Practical Considerations for Clinical Use

Place in Dry Eye Treatment Algorithm Unlike anti-inflammatory treatments, growth factors target the underlying cellular deficiencies contributing to dry eye disease.⁴ According to Dr. Perez, growth factor supplementation delivered via autologous serum tears, should be considered earlier in the treatment algorithm for dry eye disease, especially for patients with severe aqueous deficiency or those at risk for ocular surface complications. He added that even patients with milder forms of ocular surface disease might benefit from early growth factor supplementation to prevent disease progression. This approach represents a shift from using serum tears as a last resort to using them as a proactive treatment option.

Ocular Surface Disease

Dr. Pflugfelder shared that in his clinical practice, he prescribes growth factors to patients with aqueous deficient dry eye, graft vs. host disease, Stevens-Johnson syndrome, persistent corneal epithelial defects, neurotrophic keratitis, and patients with neuropathic corneal pain and has seen a range of benefts. Dr. Hamrah emphasized the regenerative properties of growth factors, describing them as a form of "regenerative therapy" for patients who have not responded to first line treatments.

Concentration and Dosing

The optimal concentration and dosing of growth factor supplements, particularly autologous serum tears, remains a subject of debate and clinical judgment. Dr. Hamrah starts with a 20% concentration of serum tears and increases to 40% if needed, noting that higher concentrations may cause discomfort in some patients and affect compliance. Dr. Chan typically starts with a concentration of 30% and occasionally increases to 40%, depending on patient response. She added that higher concentrations require more blood draws and yield less product, emphasizing the importance of balancing efficacy with patient comfort and practical considerations of product supply and cost. The panel agreed that high-quality, multicenter, placebo-controlled trials are needed to optimize the concentration and dosing regimens for different ocular surface conditions.

The duration of growth factor supplementation depends on the underlying condition and individual patient response. For chronic conditions such as severe dry eye or limbal stem cell deficiency, the panel agreed that long-term therapy may be necessary.

Even for patients with acute conditions, such as chemical injuries, Dr. Chan would consider administering maintenance therapy at a lower concentration after initial treatment with higher doses to control persistent inflammation and

stimulate healing. She also described tapering the dosing frequency for some patients who show improvement, transitioning from six times daily to a maintenance dose of two to four times daily. Dr. Hamrah added that some patients with neurotrophic keratitis might require multiple courses of treatment or long-term maintenance therapy to sustain clinical improvement.

Conclusions

In summary, the expert panel recognizes that growth factors play a critical role in maintaining ocular surface health and in promoting healing. The expert panel discussion highlighted the potential benefits of supplementation with multiple growth factors, particularly through autologous serum tears, in addressing the unique pathophysiological mechanism of growth factor deficiencies in ocular surface diseases including dry eye disease, neurotrophic keratitis, and neuropathic corneal pain.

Although more research is needed to standardize protocols and optimize treatment regimens, the clinical experiences shared by the panel suggest that integration of growth factor supplementation into treatment algorithms offers a promising approach to managing ocular surface disorders.

Financial Disclosures

Victor L Perez: Alumis, BrightStar, BRIM, Brill Engine, Claris, Dompe, Grefoil, Kala, Oculis, Santen, Sylentis, Thea

Stephen Pflugfelder is a consultant for Alcon, Dompe, Kala, Kowa and Senju and has equity interest in Unfold.

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1, 2, 3, 4. References available at *info.vitaltears.org/growthfactors*



Learn more about the role of growth factors in ocular surface disease.