

STRATEGIES FOR THE MANAGEMENT OF EYE WRINKLE REDUCTION AND UNDER-EYE PUFFINESS

Rômulo Mêne MD
Plastic Surgeon - Rio de Janeiro – Brazil

HOW TO REDUCE THE DEPTH OF LINES AND WRINKLES CAUSED BY FACIAL EXPRESSION

People have strived for years to maintain a youthful appearance, long into their mature years. When we think about a "Youthful look" we automatically picture a skin that is not wrinkled and looks **hydrated and silky, firmed and toned, radiant, smooth and without wrinkles.**

The causes of wrinkling are many, including:

- Over exposure to damaging sun
- Changes in fat content of our skin
- Changes in the skin collagen
- Dehydration

Facial wrinkling is one of the most striking signs of skin aging. Aging and photo exposure are the major explanation but secondary factors also cause **folds, furrows and creases** in facial skin. In any case, the molecular mechanism in skin aging are related to changes in of **collagen triple helix, degradation of the elastin polypeptides** and certain disorder in the packing of **lipid matrix of the skin.**

The primary problem is dehydration of the skin that results in the appearance of wrinkles. The skin has several strategies to retain moisture and thus maintain the soft and wrinkle free appearance of a youthful skin. As the skin ages or undergoes photo aging, the water retaining properties are compromised. In fact, dry skin is actually the hallmark of excessive water loss.

The skin produces a barrier that prevents water loss and a water retaining material. As the skin ages, these strategies become less effective. The barrier function of the skin is provided by a family of skin lipids that help retard the movement of water out through the skin. The production of these lipids is in decline by age 25.

By supplementing the skin with the precise mixture and type of lipids that are lost with aging, this function can be restored. (FIGS. 1A - 1B, 2A - 2B, 3A - 3B).

As the skin ages, the production of what are collectively known as the ground substances (actually the glycosaminoglycans or GAG's) are also in decline. The GAG's surround the collagen, elastin, and cells of the skin. They bind water molecules thus assisting in the hydrating of the skin proteins. They provide the water binding strategy for maintaining skin hydration. A special Serum formulation has been developed, to replenish the GAG's thus promoting the inner hydration necessary to give the skin the soft and smooth feel of a youthful skin.

Additionally, it contains a unique ingredient, an ESUP-A peptide, that helps to relax the muscles associated with wrinkles.

Its mechanism of action is similar to that of injectable Botulinum Toxin Type A that is used to treat spasmodic disorders and used cosmetically to remove wrinkles especially in the forehead.

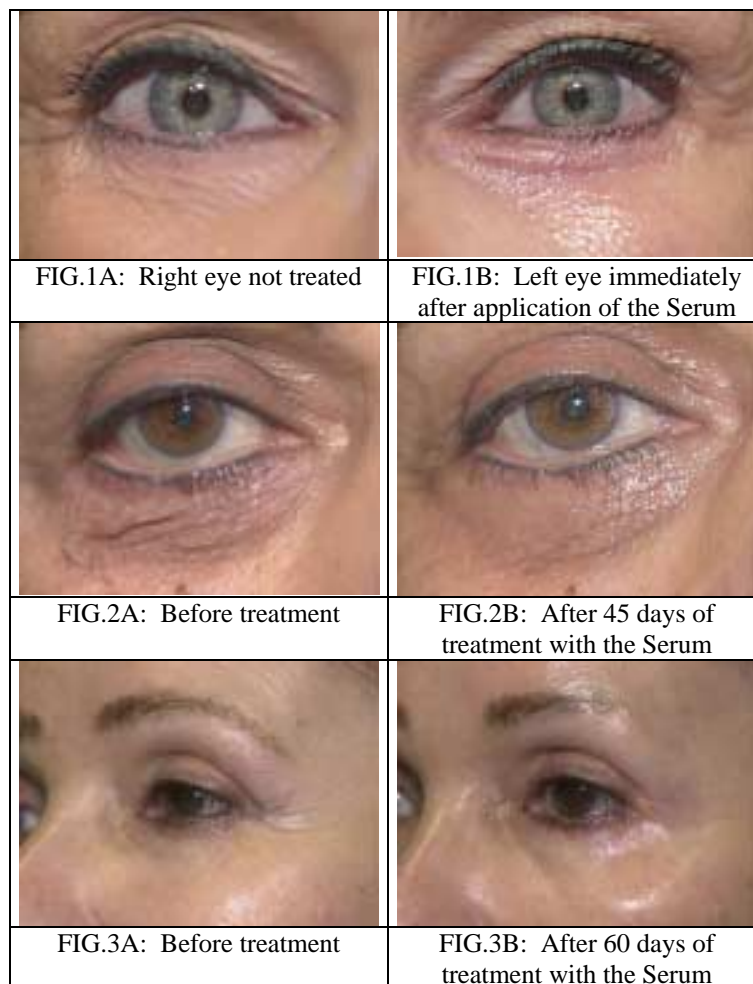
Clostridium botulinum has been a problem bacterium throughout our history although it has only been recorded as such since the 18th century. In the early 1950s, the physiology of nerve transmission demonstrated that the neurotransmitters were contained in packets (vesicles) at the end of nerve terminals at the nerve synapse. The release of these discreet packets are called exocytosis. Botulinum toxin induces paralysis by blocking the release of the neurotransmitters.

Exocytosis involves proteins, known as SNARE's, for soluble NSF attachment protein receptors. These proteins interact to form the SNARE complex that regulates the release of the neurotransmitters from the vesicles. Botulinum toxin is able to inhibit the action of the SNARE complex. Once this mechanism was understood, small portions of the SNARE proteins were studied as competitors of the SNARE complex. A small hexapeptide (6 aminoacids) was found to inhibit the vesicles from releasing the neurotransmitters thus preventing the muscle contraction.

This special formulation that combines the lipidic action and the peptide **ESUP-A** is a rich Serum (Intensive Serum W) that should be applied 2-3 times a day around the eye contour (orbicular) muscles of the upper and lower eyelid with the help if the finger tips. The visible results can be observed immediately through the capacity of the natural lipids to penetrate immediately deep into the dry stratum corneum

The relaxation of the orbicular muscle will happen between 45-60 days of treatment with this special formulation. (FIGS. 2A - 2B, 3A - 3B).

This treatment can be associated simultaneously with the injected Botulinum toxin.



HOW TO REDUCE UNDER-EYE PUFFINESS

Puffiness under the eyes of older people is usually the result of fat accumulating on the lower lids causing patients to have a tired and aged appearance. A new formulation has been developed to intervene against the array of events that contribute to the “old-looking” eyes. This is a non-surgical alternative for improving “old-looking” eyes by reducing the prominence of the bulging fat pads.

Hypertrophy of the adipose tissue is due to both an overload of triglycerides in the adipocytes and an alteration in the connective tissue due to proteolytic enzymes that enable lipid hypertrophy within the tissues. The increase in the collagenase activity, a major proteolytic enzyme, occurs from normal aging phenomena and UV stimulation resulting in:

1. The epidermis becoming thinner from reduced cell proliferation,
2. The dermis-epidermis junction is altered with disappearance of the microvilli resulting in a defective adhesion of the epidermis to the dermis, and
3. Collagen and elastin degeneration is found in the dermis.

Glycation disturbs the normal remodeling of the extracellular matrix that occurs between collagenases and inhibitors of collagenase. The effect of glycation on cell-matrix interactions is now being studied and is being shown to be an equally important aspect of ageing of collagen.

Acute puffiness of the eye is usually caused by edema but it may also be accentuated by allergies (chemical or environmental), poor blood circulation that may involve increased capillary pressure and permeability or mild irritation that can lead to the release of inflammatory mediators. Similarly, allergy resulting in edema contributes to a darkening of the eyelids, often times producing dark circles. (FIGS.4A, 5A, 6A).

The Causes: Free Radicals, Glycosylation, Senescent Fibroblasts, and Inflammatory Pigmentation

- **Glycation –**

Skin aging involves major changes in the conjunctive tissue elements of the skin. Non-enzymatic modification of tissue proteins by reducing sugars, the so-called Maillard reaction, is a prominent feature of aging. The outward manifestations of tissue ageing, occurring in the elderly, primarily involve the two major structural proteins of the body, collagen and elastin. Also inflammatory process creates many of the conditions that contribute to the development of dark circles and puffy eyes such as increased melanin deposition and increased collagenase activity respectively.

- **Free Radical Formation –**

Photoageing by UV involves the competing reactions, chain cleavage and cross-linking, the former predominating on long-term exposure. Many molecules forming the extracellular matrix are produced by the keratinocytes of the epidermis and the fibroblasts of the dermis. Those molecules include collagen, elastin, proteoglycans, fibronectin and other glycoproteins. Deterioration of this matrix plays an important role in the aging phenomenon and implies a progressive diminution in dermal

thickness, collagen content and protein organization. UV exposure stimulates the activity of collagenase activity as well as free radical formation. Free radicals adversely affect skin lipids, proteins and DNA that are critical for normal skin function.

- **Senescent Fibroblasts –**

Furthermore, the increased collagenolytic activity of senescent fibroblasts suggests that aging fibroblasts may become increasingly fibroblastic, causing many of the aging associated alterations in dermal collagen, which are observed during aging in vivo.

- **Inflammatory Pigmentation –**

There is ample evidence of the anti-inflammatory properties of alpha-melanocyte stimulating hormone (MSH). It can modulate nitric oxide synthesis as well as other inflammatory cytokines. Alpha-MSH and adrenocorticotrophic hormone (ACTH) are both synthesized in the epidermis and their synthesis is up regulated by exposure to ultraviolet radiation. Therefore, inflammatory stimuli will, inadvertently, increase the synthesis of alpha-MSH with the possibility of increased deposition of the dark pigments such as melanin.

Goals for the Formulations (Intensive Serum P/ SkinRenu):

- Moisturization
- Trophic Action on Supporting Tissue and Fibroblasts
- Reduce Inflammation
- Reduced Glycation

Key ingredients:

- Anti-oxidant Action
- Anti-inflammatory Action
- Anti- glycation Action
- Inhibition of Lipogenesis
- Activate the Lipolytic Processes
- Minimizes the Erythema /Edema
- Induced by Inflammatory Conditions
- Inhibits Insulin-Stimulated Lipogenesis
- Activation of cAMP-dependent Protein Kinase (Required for Lipolysis)
- Inhibition of the Collagenases

Based on the facts above described, formulation containing important chemical substances and proven therapeutic actions has been special formulated to be used around the eyes these substances are: **Pycnogenol, Glycosaminoglycans, Genistein, Silymarin, Algisium C.**

This formulation (Intensive Serum P) that should be applied twice a day around the eye contour with the help if the finger tips. The visible results can be observed after 2-3 weeks of treatment with this formulation. (FIGS.4A - 4B, 5A - 5B, 6A - 6B).



FIG.4A: Before treatment



FIG.4B: Female 80 y.o, after 20 days of treatment with the Serum



FIG.5A: Before treatment



FIG.5B: Female 78 y.o, after 60 days of treatment with the Serum



FIG.6A: Before treatment



FIG.6B: Male 49 y.o, after 65 days of treatment with the Serum