

# Needle work

**Dr Sotirios Foutsizoglou** on cosmetic use of mesotherapy for face and neck rejuvenation

**M**esotherapy (from Greek mesos, "middle", and therapy from Greek therapeia, "to treat medically") is the practice of using a combination of target specific microinjections into the mesoderm in order to deliver healing or corrective treatment to a variety of conditions ranging from arthritis and sports injuries to improvement of blood circulation and lymphatic drainage. Mesotherapy was founded by Dr Michel Pistor in the early 1950s and since then an increasing number of physicians have been performing treatments based on the Mesotherapy principles and techniques. Despite the lack of gold standard clinical trials regarding the efficacy of Mesotherapy - making it vulnerable to criticism by the generally more sceptical medical community - the use of allopathic and homeopathic remedies mainly as intradermal infusions has gained popularity throughout Europe (e.g. France, Germany, Spain, Greece) and South America. The French Academy of Medicine recognised Mesotherapy as a Specialty of Medicine in 1987. Mesotherapy has also been widely used for aesthetic purposes as an alternative to traditional non-surgical cosmetic treatments!

There are literally hundreds of substances that form the mesotherapy armamentarium and their use is dependent upon practitioners' preferences and experience and the problem or the area of the body being treated

At this point I would like to clarify that fat reduction using injection lipolysis (i.e. phosphatidylcholine +/- deoxycholate) is not Mesotherapy. Mesotherapy is distinct from treating adipose tissue with subcutaneous injections which usually require a depth of 6-12mm into the subcutaneous fatty tissue as opposed to intracutaneously administered injections at a depth of 1-4mm for Mesotherapy.<sup>2,3</sup> One of the fundamental principles of Mesotherapy: "Always inject superficially", i.e. preferably at the level of dermal-epidermal junction).

There are literally hundreds of substances that form the mesotherapy armamentarium and their use is dependent upon practitioners' preferences and experience and the problem or the area of the body being treated. My main focus, in this article, is to suggest some protocols for face and neck treatments based on my experience and provide the scientific background and evidence regarding the most commonly used products and solutions that every practitioner using Mesotherapy should be familiar with.

### INJECTION TECHNIQUES

There are three main injection techniques used in Mesotherapy:

- Papule
- Nappage
- Point by point (usually deeper injections used in rheumatology or sports related pathology)

#### PAPULE

Depth of injection: 1 - 2 mm

Hold the needle almost parallel to the skin

With bevel of needle facing upwards raise a small papule at the level of dermal-epidermal junction.

Suitable for treating wrinkles, scars and skin imperfections.

Papule normally fades within a few minutes.

#### NAPPAGE

Slightly deeper; 2 - 4mm

At an angle of about 60°

Series of injections 3 to 4 mm apart whilst maintaining constant pressure on the plunger.

Recommended in delicate areas where skin is too thin, e.g. perio-orbital area

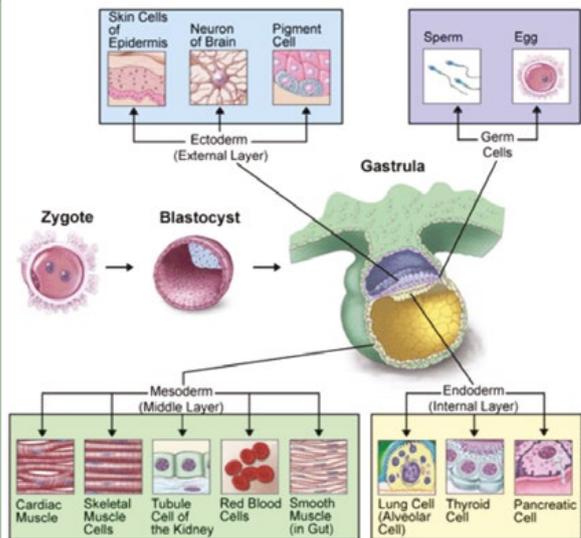
Practitioner's gloved finger may be used to aid deeper penetration of the infused product (which by now has become mixed with capillary blood) by gently massaging over treated area.

Nowadays assisted injection systems (e.g. mesotherapy guns) have been increasingly used as they provide a standardised injection depth, reduce treatment time, are easy to use and most importantly make the whole procedure better tolerated by the patient.

### AGEING AND THE ROLE OF COSMETIC MESOTHERAPY

Ageing is due to a cumulative effect of intrinsic and extrinsic factors leading to cell apoptosis. Intrinsic and extrinsic ageing are two different processes but they seem to share common biochemical and molecular mechanisms. With increasing age, a progressive deterioration of the response of the keratinocytes and fibroblasts to growth factors is detected along with a decline of their proliferative capacity contributing

### Cell differentiation



**Mesoderm** is the middle layer of the three primary germ cell layers - the other two are the ectoderm and endoderm - in the very early embryo. It differentiates to give rise to a number of tissues and structures including bone, muscle, connective tissue, and the middle layer of the skin.

to cutaneous ageing<sup>4</sup>. In addition, the repairing capacity of cellular DNA and mtDNA reduces with time. Biochemical reactions, like oxidation, hydrolysis, and alkylations can cause damage or mutation in DNA. It is estimated that every day the DNA of a cell undergoes 200,000 alterations. A complex cellular mechanism catalysed by diverse enzymatic groups is responsible for repairing the damage taking place daily in DNA and mitochondrial DNA (mtDNA) preventing mutagenic and irreversible DNA alterations that could lead to cell malfunction and death.

Intrinsic ageing comprises among other factors the following:

- **Endocrine** - neurotransmitters, thyroid hormones, melatonin, growth hormone and DHEA are reduced with ageing, whereas glucocorticoids (e.g. cortisol) increase<sup>5</sup>. These endocrine changes have a direct effect in the function of cells and also interfere with the hormonal feedback circuits in the hypothalamus-pituitary neuro axis.
- **Immunological** - with ageing, the immune system becomes less resistant to infections or diseases and less capable of discriminating between the body's own and foreign proteins.
- **Inflammatory** - it is well established that ageing is associated with an increase in cellular secretion of pro-inflammatory cytokines that induce a chronic inflammatory state<sup>6</sup>.
- **Accumulation of toxins and waste products** - with time, cellular accumulation of diverse materials of endogenous and exogenous origin such as liposoluble substances, Advanced Glycosylation End products (AGEs), protein aggregates, organic and inorganic metabolic by-products can eventually damage cellular viability leading to cell apoptosis.

**Photoageing**, the main extrinsic ageing factor, induces cellular changes and alterations of the protein matrix in the papillary dermis<sup>8</sup>, probably through repeated exposure to proteolytic enzymes released by inflammatory cells, causing fragility, loss of elasticity and poor healing. The interaction of UV light with the skin causes, among other reactions, the formation of free >

radicals<sup>iii</sup> of the ROS (=Reactive Oxygen Species) type responsible for "oxidative stress" leading to a large decrease in the reducing capacity of the cellular redox couples<sup>iii</sup>, such as glutathione. UV radiation gives rise to melanin pigment alterations and exposure to UVA induces the activation of metalloproteases which subsequently break down collagen and inhibit procollagen biosynthesis.

To date there has not been any drug, substance or treatment that can reverse or stop ageing. However medical cosmetic treatments have been successful in partial correction or reduction of symptomatic cutaneous ageing of either cause; extrinsic or intrinsic.

The aim of **Cosmetic Mesotherapy** is to break the chain of events leading to the manifestations of cutaneous ageing either by cellular replenishment of the skin (e.g. through stimulation of synthesis of collagen and proteoglycans increasing the

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thickness of the epidermis and dermis) or by rendering skin capable of fighting off damaging exogenous and endogenous mechanisms (e.g. free radical action) and increasing the speed of cutaneous regeneration.

<sup>i</sup>Collagens XII and XVI, non-fibrillar collagens specific to the papillary dermis, are responsible for skin deformability and extensibility. Oxytalan fibres are related to elastic properties of the skin. Ubiquitous collagens such as collagens I and VI are associated with the cohesion and the resistance of the dermis<sup>5</sup>.

<sup>ii</sup>A free radical is a molecule that has an unpaired electron or an odd number of electrons. It has a high reactivity or chemical instability and a high affinity to combine with an electron of any other molecule or another free radical. Because of their high reactivity, free radicals can destroy cellular viability if not appropriately neutralised.

RECOMMENDED MESOTHERAPY PROTOCOLS FOR FACE AND NECK		
Condition	Cocktail	Frequency
Mesolift (Face & Neck Lift)	Organic Silica & DMAE 2.5ml, Vitamin C 1ml, Hyaluronic acid 3.5% 3.5ml, Asian Centella 2ml, Sodium Pyruvate 1-2ml	One session per week for 6-12 weeks depending on the severity of the problem. Maintenance thereafter every 3-4 months.
Anti-ageing I	Hyaluronic Acid 3.5% 2.5ml <b>or</b> X-ADN 2.5ml, Biotin 2ml, Argireline 1ml (Botox effect), Vitamin A 1ml	One session per week for 6-12 weeks depending on the severity of the problem. Maintenance thereafter every 3-4 months.
Anti-ageing II	Asian Centella 2ml, Sodium Pyruvate 2ml, Vitamin C 1ml HA, Gel or Liquid base 2.5-3.5ml, Organic Silica & DMAE 2.5ml	One session per week for 6-12 weeks depending on the severity of the problem. Maintenance thereafter every 3-4 months
Anti-ageing III	Organic Silica 1ml, Polyvitamins with Trace Elements - 1 ampoule (2.5-5ml), Sodium Pyruvate 1ml, HA 0.3 liquid base 2.5-3.5ml	One session per week for 6-12 weeks depending on the severity of the problem. Maintenance thereafter every 3-4 months
Anti-oxidant	Pyruvate 2ml, Polyvitamins or Vitamin C 2ml, Organic Silicon 2ml, +/- Asian Centella 2ml	One session per week usually for 6 weeks.
Hydration & Nourishing	Hyaluronic Acid 3.5% <b>or</b> X-DNA Gel 3.5ml, Polyvitamins 2.5-5ml, Trace Elements 1ml, Dexpanthenol 1ml	One session per week for 6-12 weeks depending on the severity of the problem. Maintenance thereafter every 3-4 months
Tired Eyes / Dark Circles	Per eye, Ginkgo Biloba 0.5ml, Caffeine 0.5ml, Organic Silica 0.5ml	One treatment per week for an average 6 week period. Treatment cycle may be longer depending on the problem.
Fat bags under eyes	Phosphatidylcholine	A few drops per eye. One treatment per week for typically 6 weeks-longer if problem more serious. When improvement can be seen the treatment can be carried out every two weeks until desired result is seen.
Pigmentation	Glutathione 3ml, Glycolic Acid 1% Vitamin C 2ml, Dexpanthenol 2ml	One treatment per week for an average 6 week period. Treatment cycle may be longer depending on the problem.
Dry skin	Biotin 1ml, Glycolic Acid 1% 1ml, Dexpanthenol 2ml, HA 0.3% liquid base 2.5-3.5ml	One session per week for 6-12 weeks depending on the severity of the problem. Maintenance thereafter every 3-4 months
Acne	Glycolic Acid 1% 1ml, Vitamin A 1ml, Trace Elements 2ml, Dexpanthenol 2ml	One session per week for 6-12 weeks depending on the severity of the problem. Maintenance thereafter every 3-4 months



\*In collaboration with Koreesa Group, the largest distributor of mesotherapy products in the UK.

<sup>iii</sup>A redox reaction involves the transfer of electrons between atoms, molecules or ions. Redox is the abbreviation of oxidation - reduction which is respectively the increase and decrease of the oxidative state of an atom, molecule, or ion that take place simultaneously during the electron transfer process.

There is strong evidence suggesting that Mesotherapy is an excellent way of providing:

- **Photoprotection** by inhibition of immunosuppression and ROS production along with protection of cellular DNA and mitochondria.
- **Anti free radical action** (e.g. Anti-oxidant vitamins: Vit. C & E; Co-enzymes such as Q-10; Trace elements such as copper, zinc, magnesium, selenium, etc).
- **Increase in the production of skin matrix proteins** (e.g. by administering amino acids or certain synthetic peptides through Mesotherapy infusion there is stimulation of dermal proteins such as collagen, elastin and glycoproteins which, to a great extent, are responsible for the biomechanical properties of the skin)
- **Whitening action** (e.g. Glycolic acid, Glutathione)
- **Increase of firmness and cutaneous elasticity** (e.g. Organic silica, Centella Asiatica)
- **Cellular proliferation, differentiation and keratinisation along with regulation of fat production** (e.g. Retinoids)
- **Anti-inflammatory and immunomodulatory properties** (e.g. Vit. A)

#### INTRINSIC CAUSES

Metabolic damage due to

- Free radicals
- Glycation
- Mutations in mitochondrial DNA

Cellular death due to

- Shortening of telomeres
- Reduction in DNA repair capacity
- Reduction in anti-oxidant defence
- Defective cellular cycles

Accumulation of toxic products due to

- Protein aggregates with cross-linkages
- Advanced Glycosylation End products (AGEs)
- Inflammatory cytokines
- Accumulation of lipofuscin-like material<sup>iv</sup>

#### EXTRINSIC CAUSES

- Solar UV light
- Atmospheric pollutant factors (e.g. dioxins)
- Tobacco smoke
- Environmental factors (e.g. ionizing radiation)
- Pesticides
- Exogenous hormonal disruptors
- Drugs

- **Inhibition of metalloproteases** (e.g. TIMP1, TIMP2, TIMP3 and TIMP4)

- **Hydration** (e.g. Hyaluronic Acid)

- **Cytokines** (e.g. synthetic oligopeptides)

<sup>iv</sup>Lipofuscin is the product of the oxidation of unsaturated fatty acids, and may be symptomatic of membrane damage, or damage to mitochondria and lysosomes. Aside from a large lipid content, lipofuscin is known to contain sugars and metals, including mercury, aluminum, iron, copper and zinc.<sup>7</sup>

#### PRODUCTS MOST COMMONLY USED IN MESOTHERAPY FOR FACE AND NECK TREATMENTS

**Dimethylaminoethanol**, also known as **DMAE**, is related to choline and is a biochemical precursor to the neurotransmitter acetylcholine, which is involved in muscle tone counteracting flaccidity. DMAE produces a cholinergic stimulation of fibroblasts, by acting on their membrane receptors, which coupled by its anti-radical and anti-lipofuscin properties along with its repairing ability on the proteinic cross linking (i.e. collagen and elastin) results in a firming and lifting effect of the skin.

#### Indications

- Neck lifting
- Flaccidity
- Sagging skin.

**Hyaluronic Acid** (also called **Hyaluronan** or **Hyaluronate**) is an anionic, non-sulfated glycosaminoglycan distributed widely throughout connective, epithelial, and neural tissues.

HA fills in the space between collagen and elastin fibres taking part in cutaneous mechanical support. Hyaluronic acid's interaction with CD44 drives collagen synthesis and normal skin function. Present in the extracellular matrix of basal keratinocytes, hyaluronic acid is critical to the structural integrity of the dermal collagen matrix.

Skin provides a barrier to the external environment and acts to prevent the ingress of infectious agents. Once injured the beneath tissues are exposed to infection therefore rapid and effective healing is of crucial significance to reconstruct a barrier function. Skin wound healing is a complex process and includes many interacting processes initiated by haemostasis and the release of platelet derived factors.<sup>9</sup> Then the following stages are inflammation, granulation tissue formation, reepithelisation and remodelling. HA is likely to play a multifaceted role in mediation of these cellular and matrix events.

It also provides a mechanism of transport of essential nutrients from the bloodstream to skin cells and is a powerful hydrating endogenous agent for the skin. The presence of hyaluronic acid in epithelial tissue has been shown to promote keratinocyte proliferation and increase the presence of retinoic acid, effecting skin hydration.

Due to its free-radical scavenging function HA protects skin against ultraviolet irradiation.<sup>10</sup> It also plays a role in angiogenesis by supporting the proliferation of endothelial >



## MESOTHERAPY PROTOCOLS

cells and thus allowing better cutaneous vascularisation.

**Indications**

- Skin hydration ● Correction of superficial wrinkles
- Skin tone and radiance ● Anti-ageing

**Organic Silica** is a water soluble and biologically active metalloid that is present in macromolecules such as elastin, collagen, proteoglycans and structural glycoproteins. It is widely used in Mesotherapy due to its diverse properties including:

- Acting as anti-oxidant to actively prevent premature ageing.
- Binding moisture in the epidermis, thus firming and strengthening the skin.
- Increasing the concentration of cAMP within adipose tissue, making possible the lipolysis and hydrolysis of the triglycerides without disturbing the cellular metabolism.
- Stimulating fibroblast mitosis, therefore increasing the biosynthesis of elastic and collagenous fibres.
- Enhancing venous capillary and lymphatic permeability improving microcirculation.

**Indications**

- Skin rejuvenation ● Cellulite ● Lipolysis
- Hair loss ● Stretchmarks ● Wound healing

**Vitamin C** (or **L-ascorbic acid** or **L-ascorbate**) forms part of the group of anti-oxidant vitamins along with vitamins A and E. It is the main non-enzymatic water soluble antioxidant of the skin being capable of rapidly scavenging a number of reactive oxygen species (ROS).

L-Ascorbate is a weak sugar acid structurally related to glucose that naturally occurs attached either to a hydrogen ion, forming ascorbic acid, or to a metal ion, forming a mineral ascorbate. Ascorbic acid performs numerous physiological functions in the human body. These functions include the synthesis of collagen (Vit. C is the co-factor in the hydroxylation process of procollagen), carnitine and neurotransmitters, the synthesis and catabolism of tyrosine and the metabolism of microsome.<sup>11</sup>

**Indications**

- Anti-oxidant ● Photo ageing ● Skin rejuvenation
- Melasma ● Wound healing ● Hair loss

**Centella Asiatica** has been documented to stimulate Type I collagen production\*. The triterpenes (asiatic acid, madecassic acid and asiaticoside) of Asian Centella stimulate collagen and elastin biosynthesis, by enhancing dermal fibroblast activity, and help to improve wound repair with a better re-epithelialisation and normalisation of perivascular connective tissue allowing an improvement of the venous wall tone and elasticity. Centella has the potential to enhance connective tissue integrity, elevate anti-oxidant levels in wound healing, and improve capillary permeability.<sup>8</sup>

**Indications**

- Anti-ageing ● Cellulite ● Scars ● Wound healing
- Venous disorders ● Dermatitis ● Skin ulcers ● Hair loss



**Sodium pyruvate** is a stable salt of the pyruvic acid. It has been found that pyruvate increases the energy available through production of glycerol from adipocytes resulting thus in enhanced lipolytic action. It has also been demonstrated that pyruvate stimulated the synthesis of collagen in the skin. Therefore it is considered an excellent energy substrate with applications in the treatment of cutaneous ageing, striae, alopecia, etc.<sup>8</sup>

\*This is the most abundant collagen of the human body. It is present in scar tissue, the end product when tissue heals by repair. It is found in tendons, skin, artery walls, the endomysium of myofibrils, fibrocartilage, and the organic part of bones and teeth.

**Indications**

- Anti-ageing ● Lipolysis
- Alopecia (in combination with Centella Asiatica, Organic Silica, etc) **AM**

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