Dermal Fillers

The solution for lines, wrinkles, lip enhancement and facial contouring.

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Tissue augmentation is a specialist area of bio-engineering which has been the subject of intrinsic research over the last twenty-five years, and represents a marriage of innovative pharmacology and chemical applications as diverse as reconstructive surgery, cosmetology, ophthalmic/ ENT and orthopaedics. In the field of cosmetic surgery, dermal filling is one of the most performed procedures. The earliest skin tissue expander or filler was autologous-fat which is today undergoing a revival, as extraction and injection methods improve.

The greatest research and successes, however, relate to connective tissue matrix material mainly collagen and hyaluronic acid, derived from non-human sources. Synthetic or semi-synthetic materials, notably polymethylmethacrylate (PMMA), gore-tex and, more debatably, silicone, also have a niche application. These latter products are marked by superior persistence and longevity in the body but carry attendant risks of complications, notably rejection, granuloma formation and scarring.

This article seeks to present a balanced review of the state of the art of some of the most commonly used fillers, namely, the two temporary fillers, namely bovine collagens and avian hyaluronic acid (HA), and the semi-synthetic semi-permanent filler PMMA - Collagen . The chemical properties, clinical applications and cautionary features of each product are described.

1 Hyaluronic acid (HA)

It is perhaps, the extradinary biocompatibility of the hyaluronan molecule that distinguishes it so markedly from other classes of materials used in soft tissue augmentation. Hyaluronan exhibits no species or tissue specificity because the chemical structure of this polysaccharide is the same throughout nature. This property has enormous benefits with respect to immunological compatability. Until recently, the most successful dermal soft tissue implants have been derived from bovine collagen whose use, because of species and tissue specificity, may be impeded by clinical reactions due to immunological incompatibility. The concept of using a hyaluronan derivative - hylan B gel (produced by a bis-ethyl-sulfonyl-crosslinking process that links every hyaluronic acid molecule into a continuous cross-linked polymer network such that the individual molecules are no longer freely soluble)[1] - for soft tissue augmentation was developed by Balazs and co-workers as a result of years of research. They established that insoluble, injectable, cross-linked hylan gels made from hyluronan exhibited a prolonged residence time in soft tissues and were as biocompatible as natural hyaluronan.

HA is injected into the dermal tissue to provide a space-occupying viscoelastic supplement for the intercellular matrix of the connective tissue. This viscosupplementation or augmentation of the dermal tissue can result in the correction of skin contour deficiencies caused by wrinkles and depressed scars.

Indications for using HA

- Nasolabial folds - the lines extending in an arc from the corners of the mouth to each outside edge of the nose.
- Oral commissures (Marionette Lines) - the lines extending down from the corners of the mouth to the jaw.

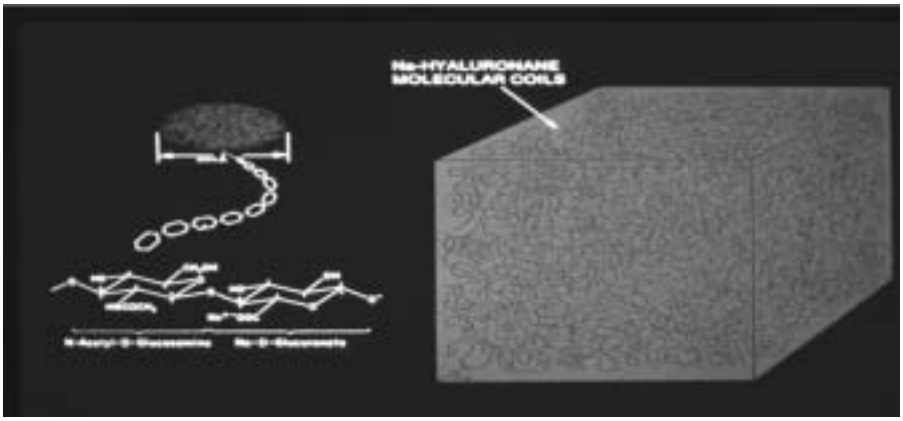

Figure 1: Hylan B gel Molecule (reproduced, with permission, from Piacquadio et al, 1998).[1]

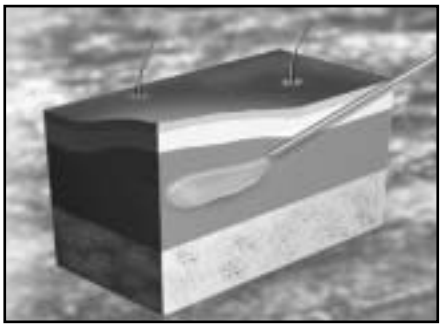

Figure 2: Tunnelling injection technique using HA (reproduced, with permission, from Piacquadio *et al*, 1998).[1]

Figure 3: Lip Augmentation using Hylan B (reproduced, with permission, from Balazs and Leshchiner, 1989).[3]

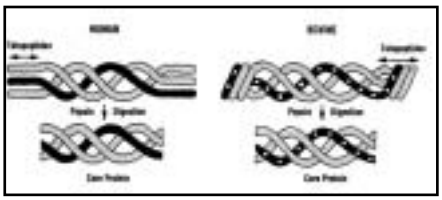

Figure 4: Similarity between human and bovine derivative (reproduced, with permission, from Balazs 1991).[5]

- Glabellar furrows (Frown Lines) - the vertical lines directly above the top of the nose and in between the eyebrows.
- Lip border - the border around the lips
- Peri-orbital - lines at the corner of the eyes
- Peri- oral - lines on the top of the upper lip.[2]

Depending on type of skin and lesion, best results are obtained in areas where these defects are readily distensible and where the correction can be visualised by manual manipulation (stretching) of the skin.

Injection procedure.

The patient has to sit upright for injection. Gravity will let the skin fall naturally so that the doctor can identify and treat the appropriate lines. The skin is stretched to provide a firm surface for injection. When injecting, the defect should not be over corrected; it should be raised to the desired level of correction. For fine wrinkles and scars it is best to place the filler in the papillary dermis. For deeper lines, the material is best placed in the reticular dermis. This can be followed by a more superficial injection into the papillary dermis to complete the treatment if needed.

For lip augmentation, the material should be injected into the apparent space between the body of the lip and the dermis of the upper lip (vermillon border) to create fuller lips (Figure 3).

Contraindications

Hylan B is contraindicated for breast augmentation, for implantation into bone, tendons, ligament or muscle. It must not be injected in patients with any acute or chronic skin disease in or near the intended area of correction.[4]

Cautions

Hylan B must not be injected into blood vessels. It may occlude the vessels, and could cause infarction or embolization.

2 Collagen

Collagen - which means glue in Greek - is a naturally occurring protein found in all mammals. It provides structural support for the bones, skin, tendons, ligaments, blood vessels, and almost every internal organ. Collagen has been used as a biomaterial in medicine and surgery for almost a century in sutures, haemostatic agents, wound dressing and heart valve replacement.

Structure And Chemical Composition

The strength and resilience of collagen is derived from the arrangement of the molecule, a rigid, triple-stranded helical structure, consisting of three polypeptide chains of 1000 amino acids wound around each other in a regular helical configuration. At both ends of the helical structure, there are short non-helical amino acid sequences known as telopeptides.

Bovine Collagen

Bovine collagen is derived from the hide of cows and is very similar in chemical composition to human collagen. The telopeptides are the regions of greatest chemical variability from species to species and consequently these sites are most likely to elicit an immune response when implanted in a foreign host. To reduce the risk of an immune response the telopeptides are removed from the bovine collagen using a protease enzyme, pepsin.

Collagen is licensed as a medical device to correct lines, wrinkles or scars. The practitioner injects small amounts of collagen directly into the dermis where the body's own collagen has been weakened by disease, trauma, atrophy, or age. The treatment restores the contour of the skin, minimising lines and wrinkles, and is often referred to as collagen replacement therapy.

Composition

Collagen is composed of highly purified sterile bovine collagen suspended in saline and 0.3% of the local anaesthetic lignocaine.

Collagen Replacement Therapy

As collagen is a naturally occurring product, it is metabolised over time. In 70% of patients the treatment has to be repeated every six to twelve months. However, 30% of patients maintain full correction for up to 12 months. For some patients this can be perceived as an advantage, as they do not have to commit to a surgical procedure that is permanent. Unlike surgery, the recovery time after collagen replacement therapy ranges from a few hours to a few days with minimal side-effects.[5]

Benefits of collagen

Collagen offers the following benefits:

- It is a simple and relatively painless procedure
- Results are almost immediate compared to other methods of skin rejuvenation and dermal correction techniques

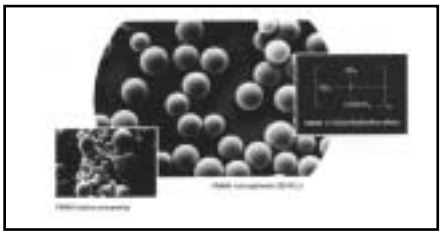

Figure 5: PMMA molecule (reproduced, with permission, from Klein, 1992).[7]

- It is associated with a low incidence of adverse reactions provided the recommended screening procedures are followed
- There is a high level of patient satisfaction with the aesthetic result

Indications for collagen replacement therapy

Collagen can be used to correct a range of facial deficiencies ranging from fine lines to deep scars and furrows. Collagen replacement therapy can also be used in combination with other treatments, such as topical retinoids, chemical peels and facial surgery and will produce excellent results.[6]

Hypersensitivity

Hypersensitivity is by far the most common adverse reaction to collagen replacement therapy, occurring in approximately three per cent of patients undergoing a test implant. A hypersensitivity reaction is characterised by erythematous, oedematous pruritic areas limited to the site of injection.[6]

Complications

These include:

- Cyst and abscess formation
- Necrosis
- Autoimmune diseases.

3 Homogenous non-biodegradable polymethylmethacrylate (PMMA) microspheres filler

Composition and mode of action

This filler is suspended in 3.5% bovine collagen and an average concentration of 0.3% lidocaine hydrochloride. The collagen serves as a vehicle for injection and is eventually degraded, leaving behind permanent implantation of the beads. All microspheres will be totally and evenly encapsulated by a fine fibrous capsule with minimal inflammatory reaction.[7] Since the PMMA microspheres are non-biodegradable, and too large to be phagocytosed or to migrate, the resulting tissue augmentation will be long lasting, if not permanent. Patients must be tested for allergy to bovine collagen prior to administration. Before using this filler, a skin test is optimally carried out 14 to 21 days prior to injection to determine the sensitivity for bovine collagen.

Injection Technique

The mixture is injected without overcorrection subdermally, that is, into the border of dermis to subcutaneous fat to treat deeper rhytids and scars. While injecting the needle should be drawn forwards and backwards (tunnelling technique) while maintaining constant pressure throughout the procedure, filling the channels thus created with the filler.[8] The injection pressure is correct if the implant flows slowly but evenly and without great exertion. The gray of the needle should never shine through the skin,

Contraindications and cautions

Contraindications to using this filler include sensitivity to bovine collagen, a history of keloids or atrophic skin diseases and patients with thin, flaccid skin because of the risk of permanent surface irregularities.[9]

The Future of Dermal Fillers

From the above, it would appear that the ideal dermal filler should:

- Be chemically and immunologically inert
- Have a space occupying effect lasting between 1-5 years, beyond which body contours are likely to alter as part of the aging process, so that the expander effect becomes less desirable
- Be easy to administer with minimal local tissue trauma

The industry is already perfecting its search for the above fillers and the most recent offerings are tissue expanders of human origin, either cadaveric or bio-engineered. Human collagen has recently obtained FDA approval and has entered clinical use this year.

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