# COLLAGEN IMPLANTATION



## THESIS

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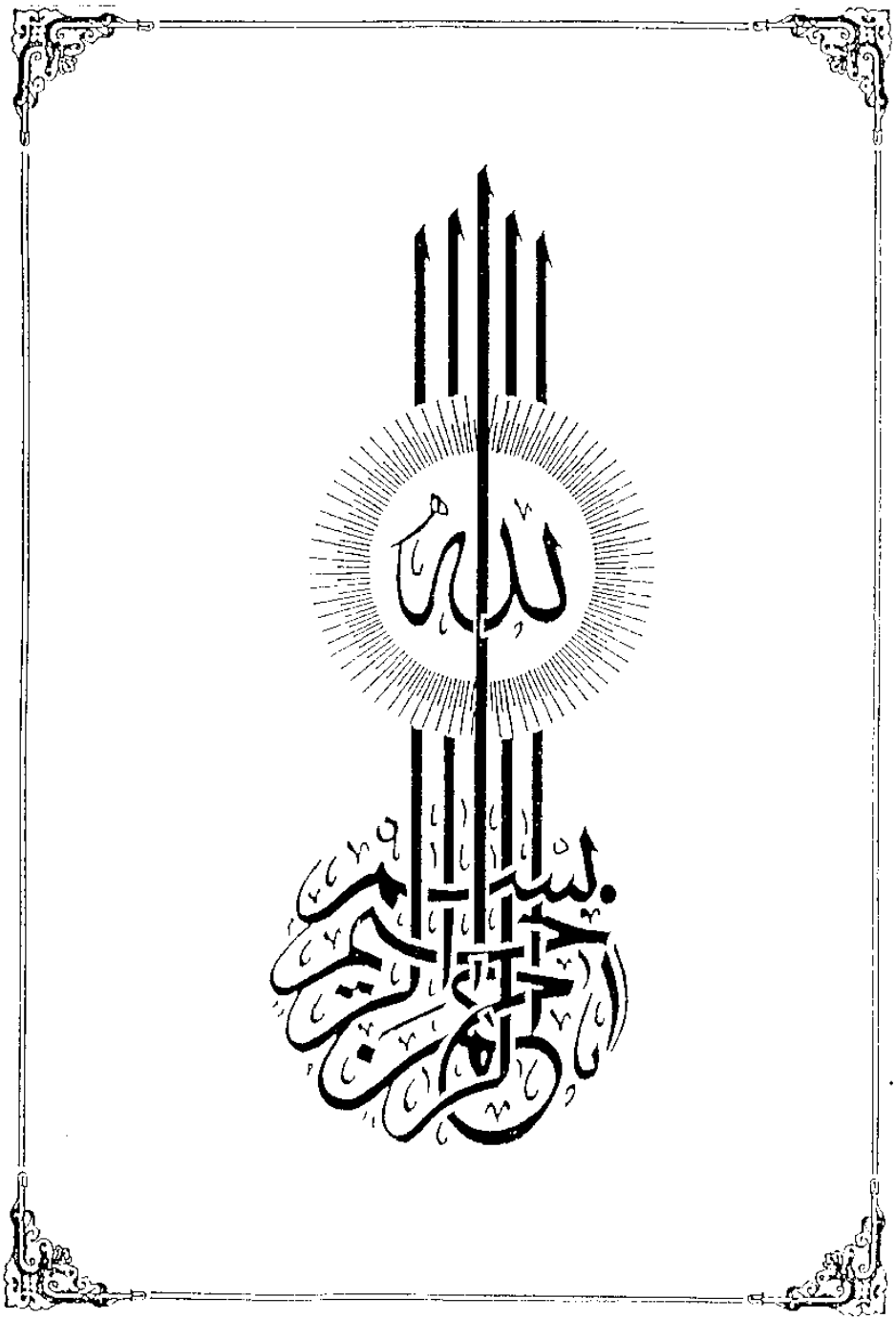

CONTENTS

## ABSTRACT

Clinical experience has demonstrated the value of injectable collagen in treating small soft tissue clefects. Among the lesions that respond best to injectable collagen therapy are nasolabial and glabellar lines as well as of atrophy and soft scars. This material is a useful adjunct to surgical procedures and can correct contour irregularities that may follow rhinoplasty. The safety of injectable collagen has also been well demonstrated.

The nature and incidance of treatment reactions (less than 3%) remains unchanged since the open of clinical triab. Reactions have been localized. All ultimately resolve without therapeutic intervention. Immunologic studies have confirmed the benign nature and specificity of reactions to injectable collagen.

# *INTRODUCTION AND AIM OF THE WORK*

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Facial Scars, lines and wrinkles represent a major problem for many people and they are difficult to be treated.

Cutaneous surgeons have paved the way in developing relatively non invasive intradermal augmentation techniques (Hanke and Robinson 1983).

The search for an appropriate material for injection into facial skin irregularities has spanned several decades. The ideal material for this purpose, in addition to be safe and effective, would be expected to be non antigenic, non irritating, non migratory and provide sustained correction (Pollack, 1990).

Soft tissue augmentation for scars and wrinkles has been practiced for years with silicone and fibrin foam. Silicone is difficult to obtain and can be responsible for long lasting and disfiguring reactions. Fibrin foam probably does not result in long lasting correction of scars and is not reproducibly successful in all physicians' hands (Kamer and Churukian, 1984).

In 1981, the Food and Drug Administration (FDA) approved for use zyderm collagen implant, an injectable sterile device derived from bovine collagen as a new line of treatment of skin disfigurement and correction of soft tissue deformities with relatively few problems and subsequently other forms of injectable collagen have become available (Knapp and Vistnes, 1985).

Zyderm collagen implant affords best correction in age induced wrinkles such as those in glabella and perioral area and it is also effective in augmenting certain types of depressed acne and surgical scars.

Adverse treatment responses are localized and self limited. They include swelling and induration (Watson et al., 1983).

The aim of this study is to throw a light on injectable collagen implantation, as regards, the history of implantable materials, importance of human collagen, preparation and chemistry of injectable collagen, its indications, techniques, immunogenicity and adverse reactions.

# *REVIEW OF LITERATURE*

# *HISTORY OF IMPLANTABLE MATERIALS*

## History of Implantable Materials

In recent decades, cutaneous surgeons have contributed to the development of numbers of implantable materials useful in the management of facial lines and wrinkles.

The most effective are injectable liquid silicone, bovine collagen implant (Zyderm/Zyplast) and fibrel foam. Each of these treatments carries its own balance of efficacy, safety and ease of use and clinicians are encouraged to evaluate each of these treatments in order to be able to offer a full range of injectable therapy for the aging face (Pollack, 1990).

In 1955, Dr. Norman Orentreich has introduced liquid silicone for treatment of skin contour irregularities and wrinkles.

Since the liquid silicone is of mineral origin and is related to sand and glass, it is not easy to ascertain its purity (Milojevic, 1982).

However, injectable liquid silicone offers distinct advantages compared to other injectable materials for correction of tissue loss, silicone might be more successful in correcting deep defects, both immediately and permanently, such as the nasolabial fold injected at the dermal fat junction in an attempt to recontour the area. But if one injects superficially, silicone can give a beaded effect and even produce a peau d'orange (orange peel) appearance to the skin, therefore the silicone must be injected at the dermal fat junction (Wilkie, 1977).

Silicone is injected through multiple (serial) punctures in "microdroplets" of volumes not greater than 0.01 ml. per injection through a 30-gauge needle on a tuberculin needle which helps the physician to accomplish this microinjection technique, and the goal should be to inject discrete microdroplets of material, separated by 1 - 2 mm. of tissue, therefore each droplet will induce its own fibroplastic response and result in added augmentation (Winer, 1964).

Although non immunogenic and chemically non reactive injected silicone is known to induce the

formation of a fibrous collagen capsule, which is produced by local cells in an attempt to "wall of" this foreign material (Orentreich and Orentreich, 1989).

Pollack (1990) stated that the injection of multiple "microdroplets" of silicon into skin irregularities yields a template of relatively high combined surface area upon which fibroplasia can take place, the stimulation of this selective deposition of collagen has proven an effective therapeutic approach to facial lines and wrinkles.

For some 35 years, injectable liquid silicone has been used to treat skin defects but until 1989, the injectable liquid silicone has never been officially approved by the (FDA) which has distanced many patients and clinicians from this modality (Orentreich and Orentreich, 1989).

The incidence of development of treatment site reactions is between 0.12% and 14% (Shelley & Hurkey, 1960). This reaction may be due to impurities of injectable liquid silicone, and the most distressing aspects of silicone reactions are the clinical appearance and the long time interval

before such reactions occur, which can take months to years to develop. The silicone reactions can appear either as firm nodular granulations or as intermittent erythema. Silicone reactions are probably a foreign body reaction rather than an allergic phenomenon (Molojevic, 1982). Histologically, foreign body giant cell reaction with mononuclear cells will be seen. In some giant cell, silicone can be seen, and cystlike spaces are present amidst the reaction (Chaplin, 1969).

Kuiper (1973) reported that the development of treatment site reaction to injectable liquid silicone has prevented its approval by (FDA) and led investigators to prefer other substances for injection such as fibrel foam with little antigenicity.

**Fibrel Foam**

Fibrel evolved from work performed some decades ago by Dr. Arther Splangler (1957), a Boston dermatologist who reported on the use of "fibrin foam" for treatment of depressed scars. In this technique, patient's plasma was mixed with a gelatin carrier and

injected beneath scars into a pocket created with a small undermining knife.

In early 1988, fibrel gelatin matrix implant was approved by (FDA) for treatment of scars, facial lines and wrinkles (Pollack, 1990).

This product is individually reconstituted for each patient treatment session in which a small amount of the patient's plasma is added to a syringe containing highly purified, denatured porcine collagen (gelatin) and epsilon-aminocaproic acid. The gelatin acts as a temporary matrix upon which the blood plasma constituents, including fibrin, are deposited and the epsilon-aminocaproic acid interferes with fibrin digestion by inhibiting production of fibrinolysin. The mode of action of fibrel is presumed to involve fibroblast activation with subsequent collagen deposition. The experimental studies have suggested that fibrin is an activator of fibroblasts (Rosen and Watkins, 1990). Spangler (1975) reported early neutrophil invasion of the fibrin foam implant followed by phagocytosis and replacement by fibroblasts, fibrocytes and normal collagen.