INTRODUCTION

There is an ongoing need to standardize scar management by establishing safe and effective treatment options that can be applied in routine clinical practice ***(Gold et al., 2014).***

Wound healing begins with coagulation then inflammation, with concomitant vasodilatation and increased vascular permeability then proliferation. Epithelial cells begin propagating from the wound edges and will complete epithelialization within 24-48 hours in most primary wound healing. Epithelialization will be prolonged if skin edges are improperly apposed during wound closure. Improper apposition or inversion inevitably leads to a scar with a visible step-off with persistent erythema from increased granulation, or that is depressed from inadequate eversion and support from deep tissue reapproximation ***(Humphrey and Thomas, 2011).***

Hypertrophic scars, by definition, represent an exaggerated proliferative response to wound healing that stays within the boundaries of the original wound, in contrast to keloids, which have a more aggressive life cycle and extend beyond the original borders. Hypertrophic scars are indurated, elevated, raised, red, nodular lesions that occur most commonly in areas of thick skin ***(Zurada et al., 2006).***

keloids appear as firm, fibrous nodules papules, or plaques, depending on the initial insult. They are often

hyperpigmented and erythematous and contain numerous telangiectasias. Many patients report pruritus or burning from their scars, particularly in younger lesions that undergo rapid growth ***(Mafong and Ashinoff, 2000).***

Prevention of keloid and hypertrophic scars remains the best strategy therefore, those patients with a predisposition to develop excessive scar formation should avoid nonessential surgery. Once a scar is present, there are many treatments from which to choose. Hypertrophic scars and keloids have been shown to respond to topical silicone, pressure therapy, intralesional injections of corticosteroid, cryotherapy, radiation, interferon and fluorouracil, and pulsed-dye laser treatment. Simple surgical excision is usually followed by recurrence unless adjunct therapies are employed ***(Alster and Tanzi, 2003).***

Silicone, a soft, semiocclusive scar cover, is composed of cross-linked polydimethylsiloxone polymer that has extensibility similar to that of skin. It minimize the size, induration, erythema, pruritus, and extensibility of preexisting hypertrophic scars and to prevent the formation of new ones ***(Zurada et al., 2006)***.

Scar laser treatments were first published in the 1980s with the continuous wave carbon dioxide (CO2), argon and neodymium-doped yttrium aluminum garnet (Nd:YAG laser. These therapies led to a recurrence or a worsening of the scarring. In the 1990s, high-energy pulsed CO2 and erbium:

YAG (Er:YAG) lasers improved the therapeutic options by causing less side effects with a wide range of indications. The short-pulsed Er: YAG laser was designed as a less aggressive alternative to CO2 lasers ***(Wagner et al., 2011).***

Pressure therapy is generally accepted as one of the best nonsurgical means of preventing and controlling hypertrophic scarring. The garments are typically custom-made from an elastic material, its mechanism of action is uncertain, but is postulated to be related to thinning of the dermis, decrease in edema, and reduction of blood flow resulting in a hypoxic environment with decreased collagen synthesis ***(Foo and Tristani-Firouzi, 2011).***

Finally, a wide range of treatment paradigms have been evaluated for the management of scarring, with most used to treat scars that have already formed. No single therapy has been universally adopted as the standard of care for clinical practice ***(Occleston et al., 2008).***

Aim of the Work

The purpose of the essay is to discuss hypertrophic scars and keloids pathogenesis and to evaluate the different modalities of treatment to successfully tackle the problem of scars.

SKIN ANATOMY

The skin (also known as the cutaneous membrane or integument) covers the external surface of the body and is the principal site of interaction with the surrounding world. In adults, the skin covers an area of about 2 square meters and weighs 4.5–5 kg, about 16% of total body weight. It ranges in thickness from 0.5 mm on the eyelids to 4.0 mm on the heels. However, over most of the body it is 1–2 mm thick. Structurally, the skin consists of two main parts the superficial, thinner portion, which is composed of epithelial tissue, is the epidermis. The deeper, thicker connective tissue portion is the dermis (Fig. 1) ***(Tortora and Derrickson, 2009).***

Deep to the dermis, but not part of the skin, is the subcutaneous layer. Also called the hypodermis which consists of loose fibrous tissue, which locally forms large accumulations of white adipose tissue. The level occupied by the secretory coils of the merocrine sweat glands conventionally defines the transition of dermis to hypodermis, fibers that extend from the dermis anchor the skin to the subcutaneous layer, which in turn attaches to underlying fascia, the connective tissue around muscles and bones ***(Van Lommel, 2003)***. The subcutaneous layer serves as a storage depot for fat and contains large blood vessels that supply the skin. This region (and sometimes the dermis) also contains nerve endings called pacinian

(lamellated) corpuscles that are sensitive to pressure ***(Tortora and Derrickson, 2009).***

During the fourth week of embryologic development, the single cell thick ectoderm and underlying mesoderm begin to proliferate and differentiate. The specialized structures formed by the skin, including teeth, hair, hair follicles, fingernails, toenails, sebaceous glands, sweat glands, apocrine glands, and mammary glands also begin to appear during this period in development. Teeth, hair, and hair follicles are formed by the epidermis and dermis in concert, while fingernails and toenails are formed by the epidermis alone. Hair follicles, sebaceous glands, sweat glands, apocrine glands, and mammary glands are considered epidermal glands or epidermal appendages, because they develop as downgrowths or diverticula of the epidermis into the dermis ***(Moore and Persuad, 1988).***

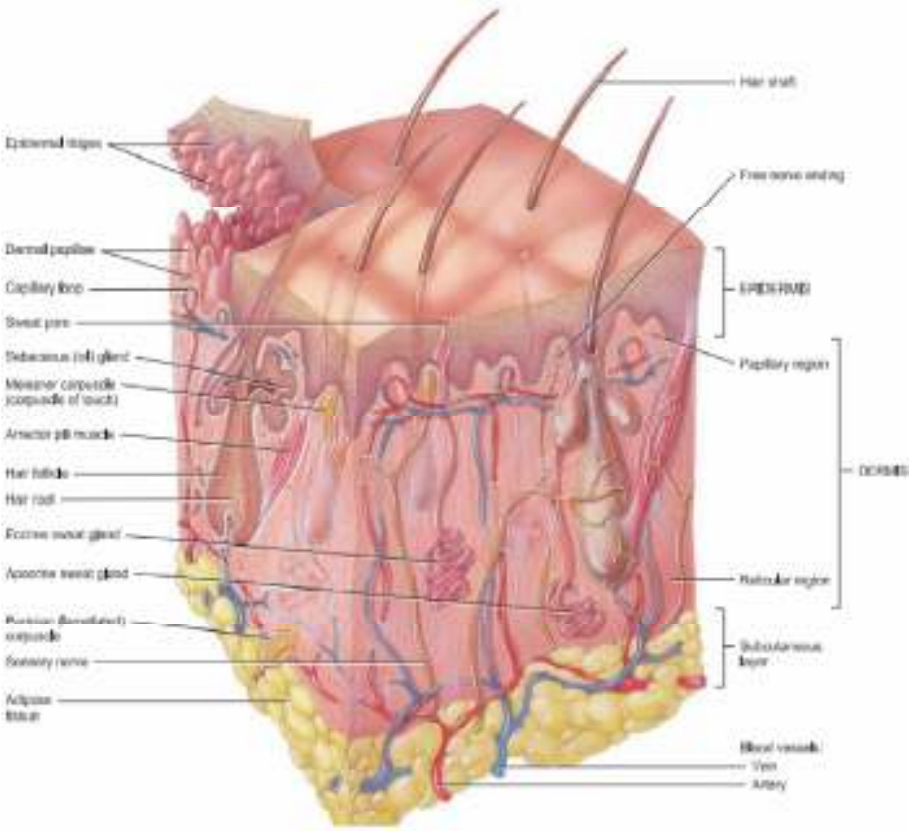

Figure (1): Sectional view of skin and subcutaneous layer
(Tortora and Derrickson, 2009).

Epidermis:

The epidermis depends entirely for the blood supply on the underlying dermis for nutrient delivery and waste disposal via diffusion through the dermoepidermal junction. The epidermis is a stratified squamous epithelium that consists primarily of keratinocytes in progressive stages of differentiation from deeper to more superficial layers. The named layers of the epidermis include the stratum germinativum, stratum spinosum, stratum granulosum, and stratum corneum (Fig.2). The stratum

germinativum or the basal layer is immediately superficial to the dermoepidermal junction. This single cell layer of keratinocytes is attached to the basement membrane via hemidesmosomes ***(Cui et al., 2011).***

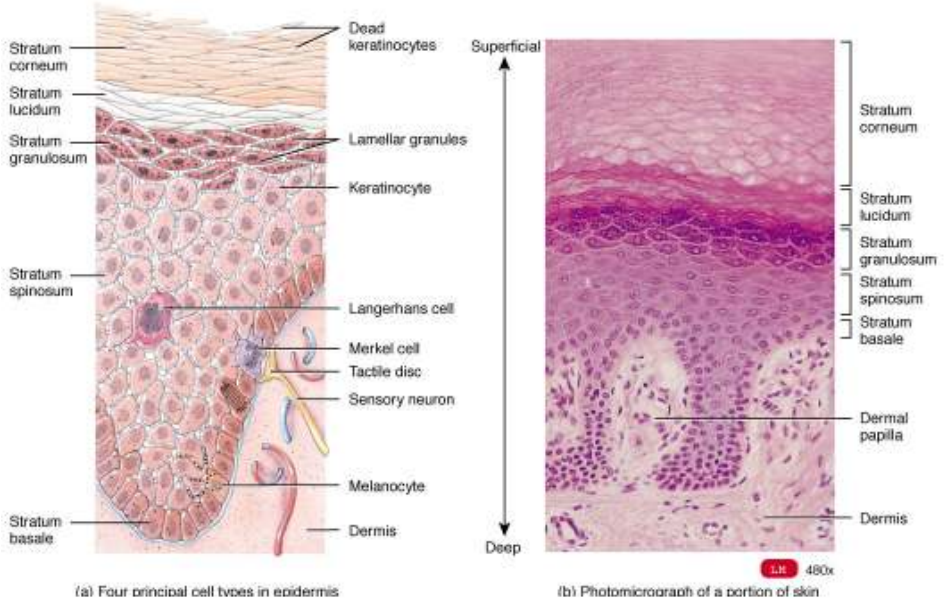

Figure (2): Layers of the epidermis ***(Baranoski and Elizabeth, 2008).***

As keratinocytes divide and differentiate, they move from this deeper layer to the more superficial layers. Once they reach the stratum corneum, they are fully differentiated keratinocytes devoid of nuclei and are subsequently shed in the process of epidermal turnover. Cells of the stratum corneum are the largest and most abundant of the epidermis. This layer ranges in thickness from 15-100 or more cells depending on anatomic location and is the primary protective barrier from the external environment ***(Burns, 2004).***

Melanocytes, derived from neural crest cells, primarily function to produce a pigment, melanin, which absorbs radiant energy from the sun and protects the skin from the harmful effects of ultraviolet radiation, Melanin accumulates in organelles termed melanosomes (Fig. 3) that are incorporated into dendrites anchoring the melanosome to the surrounding keratinocytes. Ultimately, the melanosomes are transferred via phagocytosis to the adjacent keratinocytes where they remain as granules, Melanocytes are found in the basal layer of the epidermis as well as in hair follicles, the retina, uveal tract, and leptomeninges. These cells are the sites of origin of melanoma ***(Graaff, 2001).***

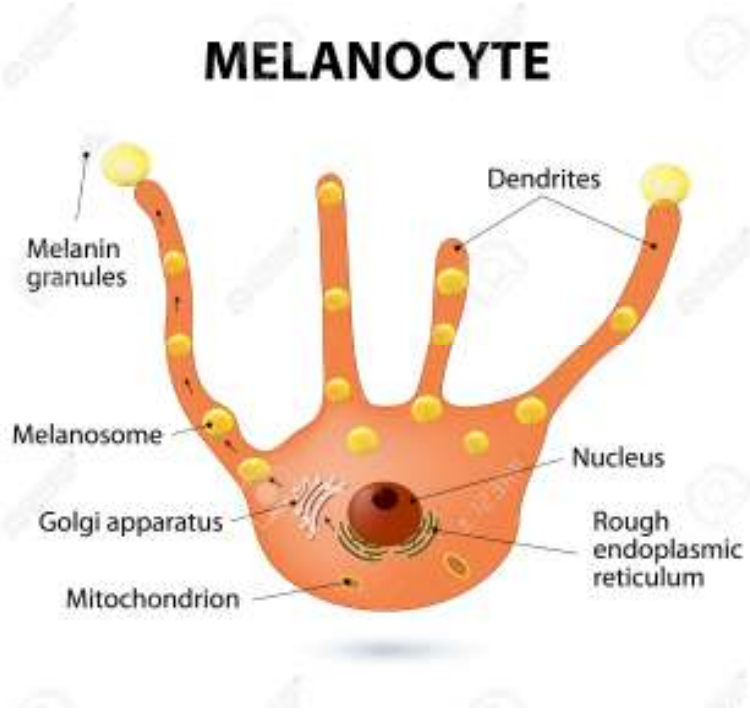

Figure (3): Melanocyte ***(Vincent and Stanley, 2008).***

In areas exposed to the sun, the ratio of melanocytes to keratinocytes is approximately 1:4. In areas not exposed to solar radiation, the ratio may be as small as 1:30. Absolute numbers of melanosomes are the same among the sexes and various races. Differing pigmentation among individuals is related to melanosome size rather than cell number. Sun exposure, melanocyte-stimulating hormone (MSH), adrenocorticotropic hormone (ACTH), estrogens, and progesterones stimulate melanin production. With aging, a decline is observed in the number of melanocytes populating the skin of an individual. Since these cells are of neural crest origin, they have no ability to reproduce ***(Burns, 2004).***

Langerhans cells originate from the bone marrow and are found in the basal, spinous, and granular layers of the epidermis. They serve as antigen-presenting cells. They are capable of ingesting foreign antigens, processing them into small peptide fragments, binding them with major histocompatibility complexes, and subsequently presenting them to lymphocytes for activation of the immune system. An example of activation of this component of the immune system is contact hypersensitivity ***(Schuler, 1991).***

Merkel cells, also derived from neural crest cells, are found on the volar aspect of digits, in nail beds, on the genitalia, and in other areas of the skin. These cells are specialized in the perception of light touch ***(Burns, 2004).***

Dermis

The primary function of the dermis is to sustain and support the epidermis. The dermis is a more complex structure and is composed of 2 layers, the more superficial papillary dermis and the deeper reticular dermis. The papillary dermis is thinner, consisting of loose connective tissue containing capillaries, elastic fibers, reticular fibers, and some collagen. The reticular dermis consists of a thicker layer of dense connective tissue containing larger blood vessels, closely interlaced elastic fibers, and coarse bundles of collagen fibers arranged in layers parallel to the surface ***(Parthasarathy et al., 2007).***

The reticular layer also contains fibroblasts, mast cells, nerve endings, lymphatics, and epidermal appendages. Surrounding the components of the dermis is the gel-like ground substance, composed of mucopolysaccharides (primarily hyaluronic acid), chondroitin sulfates, and glycoproteins. The deep surface of the dermis is highly irregular and borders the subcutaneous layer, the panniculusadiposus, which additionally cushions the skin ***(Thomas and Kumar, 2013).***

The fibroblast is the major cell type of the dermis. These cells produce and secrete procollagen and elastic fibers. Procollagen is terminally cleaved by proteolytic enzymes into collagen that aggregates and becomes cross-linked. These tightly cross-linked collagen fibers provide tensile strength and resistance to shear and other mechanical forces ***(Parthasarathy et al., 2007).***

Collagen makes up 70% of the weight of the dermis, primarily Type I (85% of the total collagen) and Type III (15% of the total collagen) ***(Burns, 2004).***

Elastic fibers constitute less than 1% of the weight of the dermis, but they play an enormous functional role by resisting deformational forces and returning the skin to its resting shape ***(Carlson, 1994).***

Accessory structures of the skin:

Hair

Each hair is composed of columns of dead, keratinized epidermal cells bonded together by extracellular proteins. The shaft is the superficial portion of the hair, which projects above the surface of the skin. The root is the portion of the hair deep to the shaft that penetrates into the dermis, and sometimes into the subcutaneous layer. The shaft and root of the hair both consist of three concentric layers of cells: medulla, cortex, and cuticle of the hair (Fig. 4). The inner medulla, which may be lacking in thinner hair, is composed of two or three rows of irregularly shaped cells. The middle cortex forms the major part of the shaft and consists of elongated cells. The cuticle of the hair, the outermost layer, consists of a single layer of thin, flat cells that are the most heavily keratinized. Cuticle cells on the shaft are arranged like shingles on the side of a house, with their free edges pointing toward the end of the hair ***(Tortora and Derrickson, 2009)***.

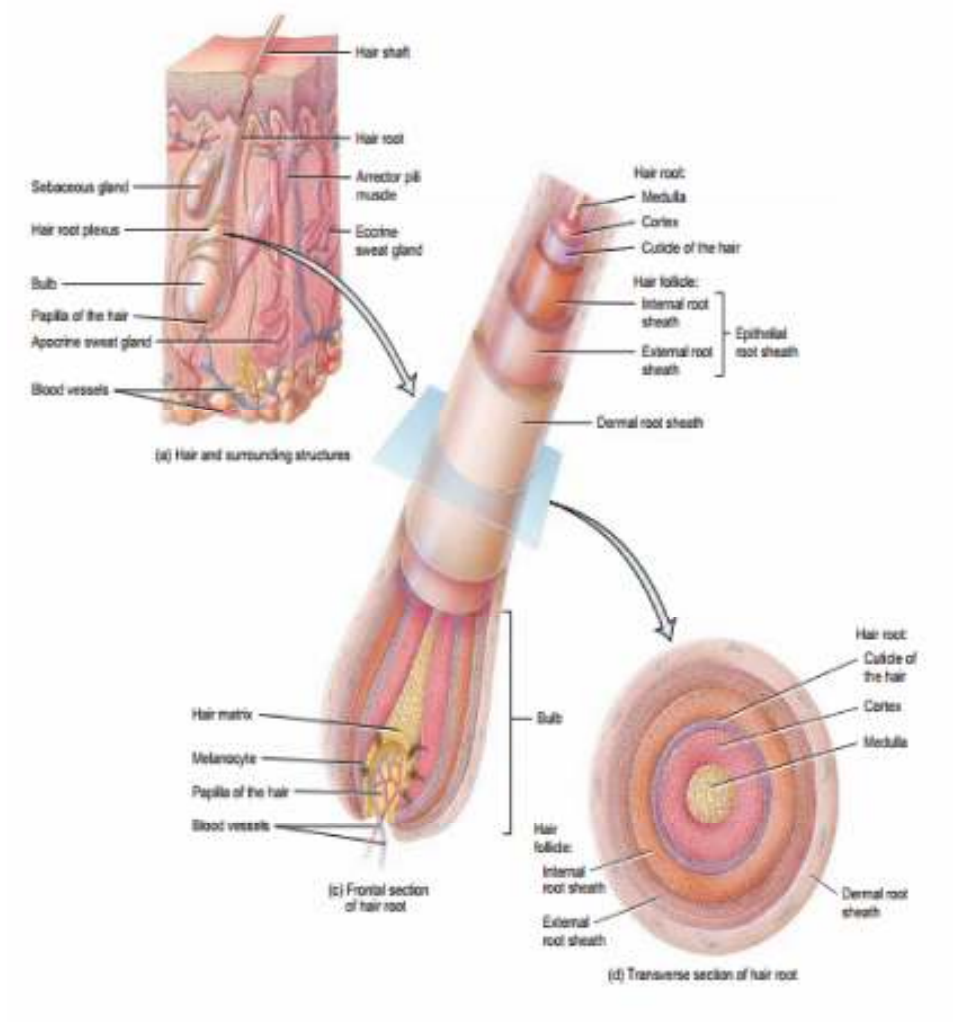

Figure (4): Anatomy of the hair ***(Tortora and Derrickson, 2009)***.

The Structural Basis of Skin Color

Melanin, hemoglobin, and carotene are three pigments that impart a wide variety of colors to skin. The amount of melanin causes the skin's color to vary from pale yellow to reddish brown to black. The difference between the two forms of melanin, pheomelanin (yellow to red) and eumelanin (brown

to black), is most apparent in the hair. Melanocytes, the melanin producing cells, are most plentiful in the epidermis of the penis, nipples of the breasts, area just around the nipples (areolae), face, and limbs. They are also present in mucous membranes. Because the number of melanocytes is about the same in all people, differences in skin color are due mainly to the amount of pigment the melanocytes produce and transfer to keratinocytes. In some people, melanin accumulates in patches called freckles. As a person ages, age (liver) spots may develop. These flat blemishes look like freckles and range in color from light brown to black. Like freckles, age spots are accumulations of melanin. A round, flat, or raised area that represents a benign localized overgrowth of melanocytes and usually develops in childhood or adolescence is called a nevus, or a mole. Melanocytes synthesize melanin from the amino acid tyrosine in the presence of an enzyme called tyrosinase. Synthesis occurs in an organelle called a melanosome. Exposure to ultraviolet (UV) light increases the enzymatic activity within melanosomes and thus increases melanin production. Both the amount and darkness of melanin increase upon UV exposure, which gives the skin a tanned appearance and helps protect the body against further UV radiation. Melanin absorbs UV radiation, prevents damage to DNA in epidermal cells, and neutralizes free radicals that form in the skin following damage by UV radiation. Thus, within limits, melanin serves a protective function. Exposing the skin to a small amount of UV

light is actually necessary for the skin to begin the process of vitamin D synthesis. However, repeatedly exposing the skin to a large amount of UV light may cause skin cancer. A tan is lost when the melanin-containing keratinocytes are shed from the stratum corneum ***(Igarashi et al., 2005).***

Dark-skinned individuals have large amounts of melanin in the epidermis. Consequently, the epidermis has a dark pigmentation and skin color ranges from yellow to reddish-brown to black. Light-skinned individuals have little melanin in the epidermis. Thus, the epidermis appears translucent and skin color ranges from pink to red depending on the oxygen content of the blood moving through capillaries in the dermis. The red color is due to hemoglobin, the oxygen-carrying pigment in red blood cells ***(Eldridge et al., 1993).***

Sebaceous Glands

Sebaceous Glands are simple, branched acinar glands, sessile or with a very short duct, which most often arise from the epidermis of a hair follicle, although solitary sebum glands are not rare. A sebum gland's peripheral cells are undifferentiated keratinocytes, they are connected to hair follicles. The secreting portion of a sebaceous gland lies in the dermis and usually opens into the neck of a hair follicle (Fig. 5). In some locations, such as the lips, glans penis, labia minora, and tarsal glands of the eyelids, sebaceous glands open