MANAGEMENT OF KELOIDS BY RADIOTHERAPY

A Thesis
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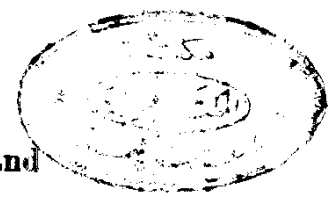

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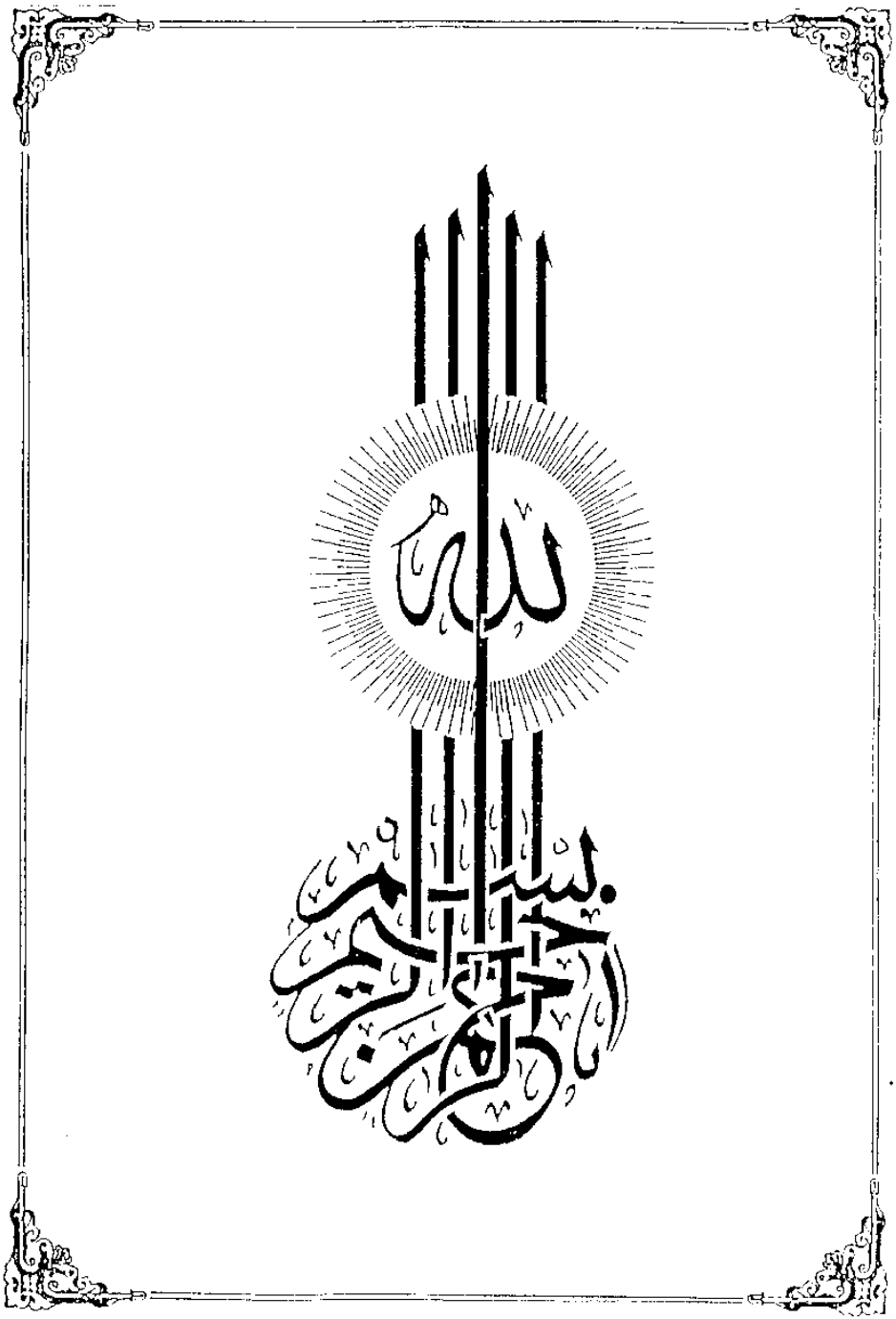

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INTRODUCTION

INTRODUCTION AND AIM OF THE WORK

Keloid scars is a complaint of dark skinned orientals and negroes more than blands. It occurs more commonly in females, but it affects both sexes at any age with a peak in the second and third decades. It is most troublesome in its early stages when still active before its duration is six months when it produces untolerable iching many workers in radiotherapy and plastic surgery have tried to find out the aetiology and curative treatment, and so several modes of treatment were described.

Our work is a comparative study to find the best curative treatment for keloid. New combinations of treatment are used. The age, sex and site incidence and cause of the keloid were also studied.

A N A T O M Y

NORMAL SKIN

Epidermis:

The normal skin is composed of two distinct portions: an epithelial portion called epidermis and a connective tissue portion called dermis.

The Epidermis:

The epidermis is a purely cellular tissue in which there is constant slow movement from inside outwards. The cells composing this tissue are the epidermal keratinocytes, their principale function is to form fibrous protien; keratin.

In normal skin the border between the epidermis and dermis is irregular because of the numerous cone shaped dermal papillae reaching up and indenting the inner surface of the epidermis. The ridges of the epidermis separating the dermal papillae are reffered to as rete pegs.

Two types of cells occur in the basal cell layer, these are the basal cells and melanocytes.

Basal cells:

These are columnar cells which lie with their axis vertical to the dividing line between the epidermis and

dermis. They have a deep basophilic cytoplasm and a dark staining oval or elongated nucleus.

The basal cells are united to one another and to the overlying cells by intercellular bridges or desmosomes. Electron microscopic examinations have clarified the nature of these intercellular bridges (Odland, Hibbs and Clark, 1959). Each desmosome is formed by two opposing protrusions of the cell membranes of neighbouring epidermal cells. These protrusions which are called attachment plaques, show considerable electron density. Each pair of attachment plaque is separated by narrow space filled with a material posessing slight electron density. From each attachment plaque arises a tuft of tonofibrils extending into the cytoplasm of the cell. At the base of the basal cells no full desmosomes are present. Instead, the tonofibrils arise from special structures of the cell membrane, the half desmosomes. The half desmosomes also attach the basal cells to the basement membrane.

Mitotic figures denoting cellular division are present in some of the basal cells. It seems that in the normal epidermis mitotic division is limited to the

basal layer (lever, 1967). Mitotic figures that appear to be located at a level above the basal layer on further sectioning are found either to be located in juxta position with a dermal papilla or to represent a division that had been initiated in the basal layer just prior to upward displacement of the cell(Van Scott and Ekel, 1963). However, during periods of regeneration of the epidermis at the margin of wounds and in certain dermatosomes mitotic activity may be found throughout the squamous layer (Sullivan and Epstein; 1963, Weinstein and Van Scott,1965). The number of mitosis present is related to the rapidity of upward movement of the epidermal cells from the basal to the horny layer. Rothberg et al.,(1961) by giving glycine C^{14} systemically to human subjects and measuring the specific activity of glycine incroporated into protiens of the hormy layer, found the turnover time of the normal epidermis to be 26 - 28 days. Epstein and Maibach, (1965), on labeling nuclei by the intradermal injection of tritiated thymidine, found that the average transit of labeled nuclei from the basal to the granular layer in human epidermis was 17.4 days varying from 12.4 to 25.6 days in individual humans. They found that the labeled nuclei migrated at differing speeds, so that

some of the labeled nuclei reached the granular layer within one week where as the last took up to 6 weeks. They concluded that the intercellular bridges, in particular at the attachment plaques are not permanent fixtures but disintegrate and reform, a characteristic that allows the epidermal cells to alter their size, shape and movement.

A subepidermal zone appears on staining with periodic acid-Schiff stain (P.A.S.) as a thin homogenous band at the dermal epidermal junction indicating the presence of a relatively large amount of neutral polysaccharides in this zone (Stoughton and Wells, 1950). Furthermore, Foots stain for reticulum demonstrates in the uppermost dermis a meshwork of reticulum fibres. Staining with alcian blue, which stains the band of polysaccharides as well as the reticulum meshwork, reveals that the band of polysaccharides is located above the reticulum layer (Cooper, 1958).

The broad heterogenous basement zone is submicroscopic when seen by the electron microscope it is only 350 . A thick and is a true membrane (Montagna, 1962).

The firm attachment of the epidermis to the dermis can be attributed to 2 factors:

1. The interlocking of the irregularly shaped cytoplasmic processes of the basal cells with corresponding dermal processes.
2. The attachment of the basal cells to the basement membrane by half desmosomes.

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MELANIN AND COLOUR OF SKIN

The colour of the human skin is produced by four pigments:

Melanin in the basal layer of the epidermis, carotene which is yellow present in the dermis, oxy-heamoglobin in the dermal capillaries and carboxy-heamoglobin in the dermal venules. Melainin is far the - most important in determining the skin colour and in guarding it from ultraviolet light.

Melanin is the protien bound pigment synthetised in melanocytes, its colour ranges from the yellow colour in the reduced state to the brown colour in the oxidised state. Melanin also affects the colour of the skin by its location, the more superficial it is, the more darker its appearance (Mansor H.S. 1959, 1966).

It must be noted that the skin colour is largely determined not by the number of melanocytes but by their manner of synthetizing and distributing melanin and whether the melanin remains intact after its transfer to Keratinocyte, (Sazabo G. et al., 1969, Horily et al., 1968, McGurie, J. 1965, Szbo, G. et al., 1972).

Melanocytes and Melanin Synthesis:

In sections stained by heamatoxylin and eosin melanocytes appear as clear cells having a small dark staining nucleus, and as a result of shrinkage clear cytoplasm. They are found wedged inbetween the basal cells of the epidermis. However, not all clear cells seen in routine sections necessarily are melanocytes since occassionally basal cells may show the same shrinkage and then are indistingiushable from melanocytes (Clark et al., 1961).

The number of melanocytes per square millimeter varies from a maximum of 2000 on the malar prominence to half this number on the trunk (Fitzpatrik, T.B. and Szabo 1959, Szabo, G. 1959).

There is no significant difference in the density of distribution of melanocytes between Negroes and Caucasians, only the activity is greater in Negroes skin (Lerner 1955, Starric and Pinkus 1957, Fitzpatrik and Szabo 1959).

The melanocytes develop as a result of maturation of the melanoblasts which are derived from the neural crest.

Melanocytes form 20 % of the basal layer of the epidermis (Szabo, G. 1959). It may be regarded as a unicellular gland producing melanin and excreting it into keratinocytes along the dendrites. Electron microscopic study reveals melanocytes to be rich in organelles but to have no tonofibrils or desmosomes. They show dendretic processes extending into the spaces between keratinocytes. On the basis of autoradiographic studies Zelickson et al. 1964 & 1950 have concluded that the synthesis of melanin from tyrosin by the action of tyrosinase in the presence of reduced copper takes place in the endoplasmic reticulum and that melanin is then transferred to the melanosomes where it unites with protien to become melanoprotien. Other authors however like Seijet et al. (1963) and Seiji and Iwatsfita (1965), and Fitzpatrick T.B. et al. 1944 by determining enzyme activity with dopa C^{14} in fractionate cell component have concluded that tyrosinase is synthetised in ribosomes, then transferred to Golgi area through the endoplasmic reticulum where it enters the melanosomes in which melanin is synthetized by the action of tyrosinase enzyme on tyrosine and unite with protien. The melanosomes in its gradual growth accumulates more and more; melanoprotien develops into a melanin granule.

In this process it loses its enzyme activity so that fully developed melanin granule is tyrosinase and dopa negative and can be regarded as an effected melanosome (Fitzpatrick 1952). Normally the melanocytes stain with Blochsdopa reaction because they posess the ability to form melanin and stain with silver because they contain melanin.

Hormones specially steroids affect pigmentation in man, but the most potent hormones affecting pigmentation are the alpha and beta melanocyte stimulating hormone M.S.H. of the pituitary gland (Lerner, A.B., 1961). The adrenotrophic hormone A.C.T.P. resembles the Alpha and Beta M.S.H. in some of their peptide sequences and can produce hyperpigmentation in men through stimulating melanogenesis.

The Squanmous Cell Layer:

The cells of the squamous layer are polygonal and form a mosaic. They become flattened towards the surface. The cells are separated by spaces that are traversed by intercellular bridges.

Examination of the epidermis with the polarizing microscope reveals in the cytoplasm of basal and squamous cells numerous doubly refratile tonofibrils forming a