HISTOLOGICAL PICTURE OF SKIN IN HUMAN FOETAL FINGER TIP

THESIS

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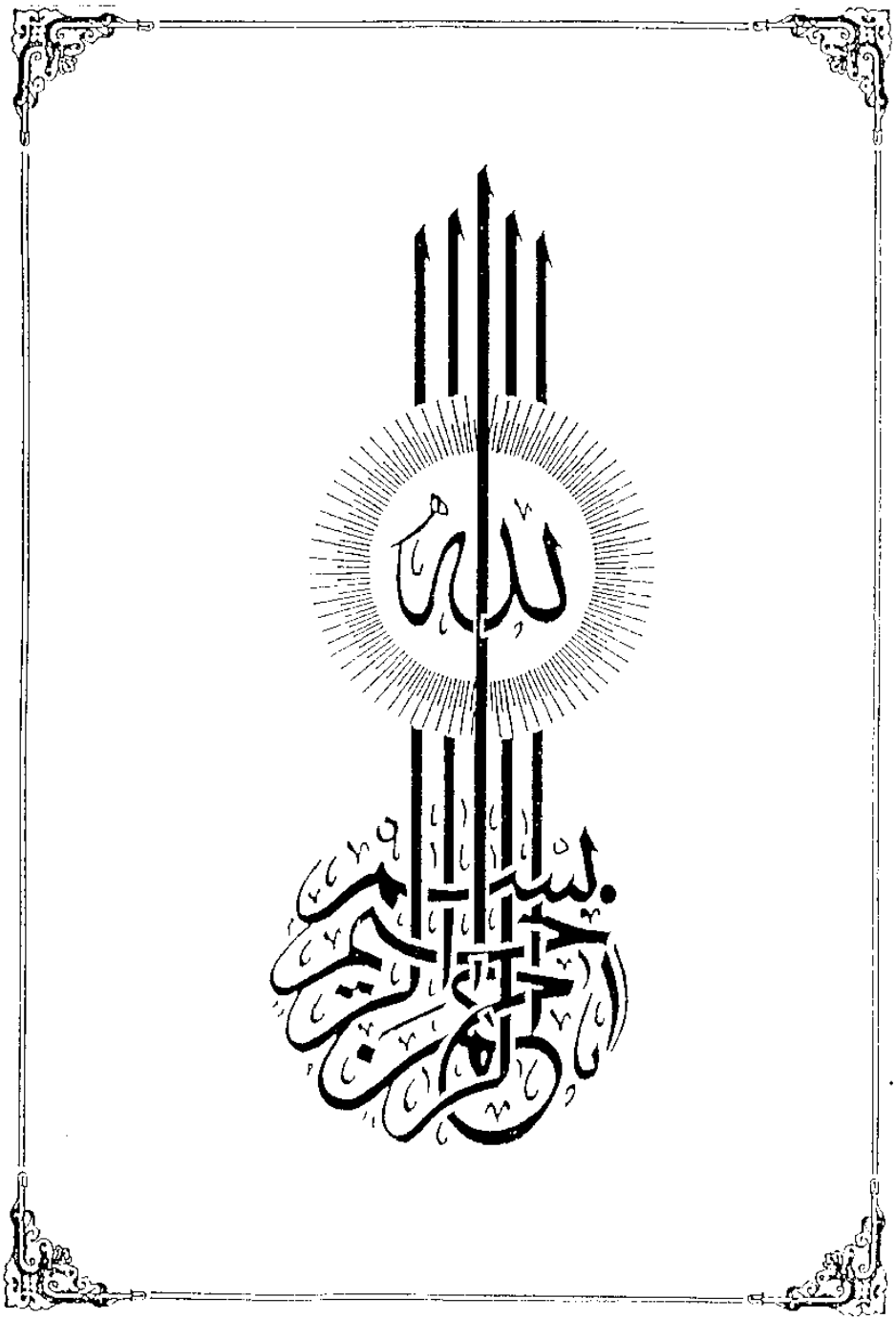

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The histology of the skin is probably best studied where it attains its greatest degree of development, the palm of the hand and particularly the palmar surface of the index finger *[Valdes Dapena , M.D., 1979]* .

Morphological characteristics of foetal skin may proove to be valuable criteria for the prenatal diagnosis of inherited skin disease. By knowing the thickness of epidermis, the stage of differentiation ,the kindes of epidermal cells and the development of various dermal elements characteristic for a foetus of a given age. *[Holbrook and Odland , 1980]*.

The aim of this work is to throw some light on the histology of the skin during intra-uterine life , in an area where it attains its best development .

REVIEW OF LITERATURE

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I. EMBRYOLOGY

The skin is of double origin. The stratified. squamous epithelium, or epidermis is derived from the general ectoderm. The fiberous layer, or dermis is usually considered to have evolved from cells proliferated from the lateral walls of the paired somites. However, it is likely that much of the dermis differentiate from non specific mesenchyme subjacent to the epidermis. Most of which comes from lateral sheets of somatic mesoderm.

The epidermis first appears as embryonic ectoderm in the form of a single sheet of cuboidal cells. In the fifth week, a second layer is added. The outer layer is distinct but transitory and is reffered to as the periderm. Its cells flatten, cornify and eventually spread to several times the diameter of the deeper cells. The basal cells remain cuboidal. During the 3rd and 4th month, the epidermis is typically 3-layered, an intermediate stratum being gradually interposed between the basal and periderm cells.

After the 4th month the epidermis becomes increasingly stratified and specialized. The lower layers consist of living cells and the upper layers constitute the "dead skin". The basal cells and their immediate descendents in

the layer just above, the stratum germinativum, are the actively dividing elements.

Pigment granules appear in the cells of the stratum germinativum of all races. They are obtained by transfer from the processes of the melanocytes. These cells migrate from the primitive neural crest tissue, invade the basal layer of the epidermis, and specialize in pigment formation. Pigment development is incomplete at birth. Hence there is marked darkening of the skin of the black infant during the six or eight weeks after delivary .

The plane of union between the epidermis and dermis is smooth until early in the 4th month, when epidermal thickening grow down into the dermis of the palms and soles. About 2 months later, in the sixth month, corresponding elevations first appear on the skin surface. These epidermal ridges complete their permanent, individual surfaces [e.g. finger prints] in the second half of foetal life.

Collagenous fibres of the dermis appear in the 3rd month, and elastic fibres in the 5th month. The differentiation of collagenous fibres occurs in two phases; the first is marked by the appearence of thin fibrils resembling those of reticular tissue . In the 3rd month those fibrils become arranged parallel to one another, and

agregate into wavy bundles with the physical and chemical characteritics of collagen.

Elastic fibres differentiate later, in the 5th month, but in the same general manner. Typically, they remain as solitary, coarse fibres which branch and anastomose. They consist of elastin, which is different from collagen both chemically and physically.

Only gradually does distinction between the compact dermis and the looser, subcutaneous tissue become recognizable. Columnar papillae project upward from the dermis into the stratum germinativum, some contain blood vessels, and others contain nerve endings. Some of the dermal cells acquire pigment granules.

Fat develops in the subcutaneous layer, but does not become abundant until the later months of foetal life. *[Arey, 1974 and Valdes-Dapena, 1979].*

II. HISTOLOGY OF SKIN

A) Epidermis :

Billingham and Medawar [1953] studied foetal skin, stated that among the epidermal cells 2 types of non keratinizing cells i.e. Melanocytes and Langerhan's cells were present in fully developed epidermis and they had also been seen at certain foetal stages. They suggested that the Langerhan's cells were the definit relict of a previously active melanocyte which had exhausted its capacity for melanogenesis.

Zimmermann and Becker [1959] stated that Melanocytes were definitly known to stem from the neural crest and to invade the epidermis at a stage of development much later than 6 weeks old embryos. They added that in Negro foetuses there were a rapid influx of melanocytes into the epidermis between 12-14 weeks.

Breathnach and Wyllie [1965a , 1967] showed that in 14 weeks-old embryos epidermal Melanocytes containing non melanized premelanosomes [= rood shaped granules exhibited 90°A straiation on longitudinal section] were present in the basal and lower intermediate layers of the epidermis. They added that no Melanocytes were seen in the dermis in 14 weeks-old embryos. Very few Langerhan's cells present, were

identical in appearence with those of adult epidermis, and non contained premelanosomes in the cytoplasm. They were also present in the basal and lower intermediate layers of the epidermis. By electron microscope they were positively identified by the presence of a cytoplasmic organelle characteristic for this type of cell, which was a disc-shaped granules. They added that Langerhan's cells acquired indented nucleus. They also suggested that Langerhan's cells were thought to be immigrant cells and they might be "histiocytes" functioning as epidermal macrophages.

Munger [1965] studied the skin of the opossum, described the presence of "clear cells" between basal and intermediate cell layers to be one of 3 types of cells either Amelanotic melanocytes, Merkel's cells or Langerhans cells, and they had to be differentiated by their electron microscopic features of each.

Hashimoto, Groos , Di-Bella and Lever [1966] stated that in 12 weeks-old embryos, the epidermis did not show any sign of Keratinization and that the stratum germinativum contained an abundant amount of glycogen in the intercellular spaces. Melanocytes were often detected both in the dermis and in the epidermis and they showed active melanin formation. He also investigated that in the 13 weeks-old embryos the intercellular glycogen in the stratum germinativum had either deminished or disappeared, while the

intracellular glycogen in the upper layers remained the same. While in embryos 14 16 weeks, the intracellular glycogen disappeared from the stratum germinativum and deminished in the upper layers. The cells in the upper layers began a keratinization process through formation of keratohyalin granules.

Wessels [1967] who studied the development of epidermis, stated that the plasma membrane of the ectodermal cell facing the amniotic fluid exhibited occasional cilia and small microvilli as an early stage in the development of the epidermis. Fine filamentous material was present in the form of skein parallels the basal plasma membrane. He added that this basal skein of filaments persisted until shortly before the development of basal hemi-desmosomes. He suggested that they might have a role in maintaining the columnar shape of the cells.

Hashimoto et al., [1966] and Hoyes [1968] described the periderm as being a protective covering for the underlying keratinizing layers. They suggested that they might be concerned with fluid or other exchange in one or both directions across the interface with the amniotic fluid. Its development reached a peak over a period 12-16 weeks, after which the periderm had undergone transformation into a layer of flattened squamous with purely filamentous internal structure.

Hoyes [1968] attributed to the periderm a major role in the production of the amniotic fluid during its period of maximal development, and associated its regression with the taking over of this function by the umbilical cord epithelium.

ParaKkal and Matoltsy [1968] raised the question of wheather or not the periderm became keratinzed and concluded that its final condition was different to that of the underlying stratum corneum , due to the fact that periderm cells did not produce keratohyalin.

Reed and Rothwell [1970] described the basal germinative epidermal cells in adult human using freeze-Etch preparations as being typical keratinocytes roughly spherical in shape or elongated with very large nuclei occupying about 1/3 of the total cell volume and granular cytoplasm containing tonofilaments. They differentiated Langerhan's cells from other keratinocytes by their relative rarity among the basal keratinocytes. The Langerhan's cell was found to contain little granular material but was mostly occupied by a complex system of vesicles, some of which were rod-shaped whilst others were more rounded bodies with rod-like processes "tennis-racquet-like "which were regarded as specific organelles for the Langerhan's cells.

Breathnach and Robins (1970) described Merkel's cell occupying the basal layer of the epidermis in human foetal skin, to be surrounded by a space similar to those seen in relation to melanocytes which had recently reached this situation.

Breathnach (1971 a, b,) mentioned that the bilaminar epidermis development started by the formation of two layers of surface cells, the periderm and the germinative layer. A fully differentiated desmosomes were developed before there was any evidence of cytoplasmic tonofilaments. He showed that these tonofilament first appeared opposite the sites of desmosomes and later throughout the cytoplasm.

Arey (1974), stated that after the 4th month of intrauterine life, the epidermis became stratified and specialized into stratum germinativum formed of actively dividing cells both in the basal cells as well as in the layers next above [prickle cells]. The thin stratum granulosum containing keratohyalin granules. Next higher lay the thin and clear stratum lucidum whose content was fluid eleidin. Nearer the surface, the epidermal cells flattened steadily and comprised the many layered stratum corneum. He stated that Melanocytes migrated from the primitive nerural crest tissue to the basal layer of the epidermis and became spescilized in pigment formation. He added that pigment