Part 1 General Consideration

Chapter 1 one

Structures and Functions of Skin

Skin is the largest organ in the body, covering 1.6 m^2 of surface area and accounting for approximately 16% of an adult's weight. Skin contains melanin, which makes it a fascinating organ. Melanin imparts color to the skin and it adds to the personality of an individual. The color, however, varies according to the environment and the temperature. In cold climates, the skin usually displays fair complexion, while in hot climates (tropics) the skin color varies from wheat-color to dark. Protection of skin from ultraviolet rays is directly proportional to the pigment present in epidermis. Texture of the skin also shows variation over different body parts. It is thick over the palms and soles and transforms itself into nails at the terminal of the fingers and toes whereas it is thinner over the eyelids. Similarly, variation of hair growth is significant in men and women. Scalp hair is thick in both men and women, whereas hair growth over the beard area in men is thicker. Pubic and axillary regions are covered with terminal hairs at puberty. The other parts of the body are covered with vellus hair.

There is a transition of skin to mucous membrane at the orifices, namely the mucocutaneous junctions. Some of the orifices are protected by hair that can trap the suspected particles. Thus, the skin not only serves to provide mechanical protection, but also serves the other functions as follows:

* Barrier function
* Temperature regulation
* Sensory function
* Synthesis of vitamin D_3
* Protection from harmful ultraviolet rays
* Protection against pathogenic micro-organisms by resident microflora.

The microscopic structure of the skin is characterized by the epidermis, dermis and adnexa. The two structures, namely epidermis and dermis are fastened together by the highly specialized dermoepidermal junction. Subcutis subserves to insulate these structures.

Epidermis

Epidermis is the outermost layer and varies in thickness from 0.04 mm on the eyelids, to 0.16 mm on the palms. The average thickness is 0.1 mm. It is a stratified squamous epithelum. It takes 28 days for the keratinocytes to move from the stratum basale to stratum corneum. In general, it is composed of the following 5 layers（Fig.1.1.1）.

Stratum basale/basal layer: It is the deepest layer formed by columnar cells perpendicular to the basement membrane zone. The cellular multiplication occurs in this layer.

Stratum spinosum/prickle cells layer: It

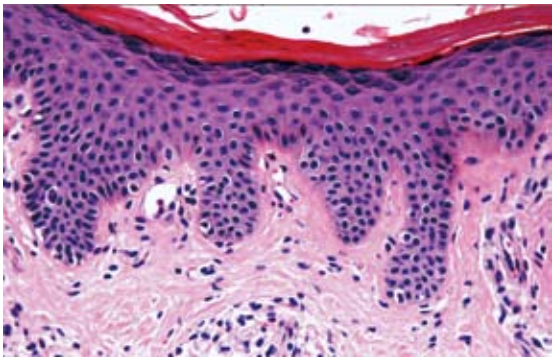

Fig.1.1.1 Epidermis

consists of 5 to 12 layers of polyhedral cells connected to one another by intercellular bridges. Areas of thickened membranes at the point of contact of adjacent keratinocytes are termed "desmosomes". There is also an intercellular cement-like substance that holds the cells together.

Stratum granulosum: It lies superficial to the prickle cell layer and is comprised of flat, fusiform cells that contain keratohyaline granules. It is 1 to 3 layers thick.

Stratum lucidum: It only appears in palms or soles where the epidermis is relatively thicker, and is comprised of transparent layers of packed dead cells.

Stratum corneum: This is the most superficial layer that consists of anucleated, flattened, cornified cells.

The cells constituting the epidermis are of the following kinds.

Keratinocytes

Keratinocytes originate from ectoderm and occupy the principal cells of the epidermis. They undergo characteristic changes during their progressively moving upward movement from the basal to cornified layer. The cytoplasm of basal keratinocytes contains abundant rough endoplasmic reticulum, ribosomes, Golgi bodies, and mitochondria. These cells actively synthesize tonofilaments which are the precursors of keratinous protein. As they ascend, more and more tonofilaments aggregate.

Within the cornified layer, aggregates of tonofilaments, rich in free sulphydryl group form a fibrous protein termed as alpha keratin; that is, embedded in the sulphur rich amorphous matrix. The amorphous protein of the matrix is derived from keratohyaline granules. These granules appear in the upper spinous layer and become prominent in the granular layer. Lamellar granules (Odland bodies) also appear in the upper spinous layer. They form bipolar phospholipids, glycoproteins, and acid phosphates. Concurrently, the nuclei and cytoplasmic organelle gradually disappear as the keratinocytes mature into cornified cells.

Melanocytes

Melanocytes are derived from the precursors in the neural crest and localized amongst basal keratinocytes. They belong to a certain kind of dendritic cells that synthesize and secrete melanin containing organelle called melanosomes. The dendrites of the melanocytes extend in all directions between adjacent keratinocytes. The ratio of the melanocytes to keratinocytes in the basal layer is about 1∶4 to 1∶10. However, in general one melanocyte is associated with an average of 36 keratinocytes. This is termed as epidermalmelanin unit. The melanin imparts color to the skin and protects it from harmful effects of sunlight by scattering and absorbing UV rays.

Langerhan's cells

They are the dendritic cells situated in the midepidermis (Fig.1.1.2). They originate from the mesenchymal precursors in the

bone marrow. They can be stained and detected by peroxidase labeled monoclonal antibody of OKT3. Ultra-structurally they are characterized by a folded nucleus and distinct intracytoplasmic organelles called Langerhan's or Birbeck granules. These granules resemble a tennis racquet. Langerhan's cells play a role in induction of graft rejection, immunosurveillance and in immune reaction of the delayed hypersensitivity type, especially allergic contact dermatitis. They also produce inter leukin-1 that is required for T cell activity.

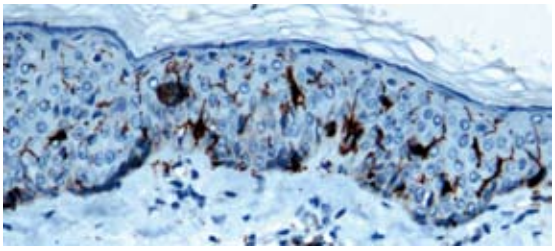

Fig.1.1.2 CD1a positive Langerhan' s cells in mid-epidermis

Merkel's cells

They are the dendritic cells that originate in the ectoderm of the neural crest. They are located above the basement membrane and contain intra-cytoplasmic neurosecretory granules. They are supplied by myelinated nerves that loose their myelin sheaths near the epidermis and continue onward as unmyelinated axons surrounded by cytoplasm and basement membranes of Schwann's cells. The apposition between Merkel's cells and axon terminals exhibits features of synapses. They function as slow adapting touch receptors.

Dermoepidermal junction (DEJ)

It represents a highly specialized attachment between the basal keratinocytes and papillary dermis. It serves to: (i) attach the epidermis to the dermis, (ii) provides support, and (iii) regulates the permeability across the epidermal-dermal interface. It can be stained by periodic acid Schiff (PAS) stain that reveals the DEJ as a thin magenta colored linear band beneath the basal keratinocytes. The ultra-structure study using electron microscopy shows it to be comprised of the following layers:

* The plasma membrane of the basal keratinocytes, which is comprised of the internal and external leaflets. The internal leaflet is studded at regular intervals with electron dense thickenings called "hemidesmosomes". Furthermore, the tonofilaments within the basal keratinocytes are aligned perpendicular to the hemidesmosomes.

* Beneath the plasma membrane is an electron lucent band, 30 nm in thickness, termed as lamina lucida. It harbors sub-basal dense plaque at regular intervals, usually located beneath the hemidesmosomes. This sub-basal dense plaque is traversed by anchoring filaments.

* The basal lamina (lamina densa) lies beneath the lamina lucida. It is electron dense and measures 40 nm in thickness.

* Below the basal lamina is a fibrous zone (reticular lamina) that harbors the anchoring fibrils, type III collagen, and microfibrils.

The dermoepidermal junction is actively affected in various bullous dermatosis, namely the pemphigoid, linear IgA dermatoses, chronic bullous dermatoses of childhood, herpes gestations, and epidermolysis bullosa of the junctional type.

Adhension between keratinocytes

Desmosomes are the major junction

between the adjacent keratinocytes and can provide resistance to mechanical stresses. It's composed of an attachment plaque (mainly desmoplakin) to which keratin fibers connect.

Dermis

The dermis rests upon the subcutaneous fat and is 15 to 40 times thicker than the epidermis. It may be divided into two compartments, i.e. (i) a thin zone immediately beneath the epidermis (the papillary dermis) and around adnexa (the periadnexal dermis) and (ii) a thick zone of reticular dermis. The dermis is mainly composed of collagen, elastic fibers, and ground substance within which are embedded the nerves, blood vessels, lymphatics, muscles and pilosebaceous, apocrine, and eccrine sweat units. The constituents of the dermis are mesodermal in origin except for nerves which are derived from the neural tissue.

Cells of the dermis

Fibroblasts are the main cells of the dermis and produce collagen fibers, elastic fibers, and glycosaminoglycans. There are also small numbers of mononuclear phagocytes and lymphocytes.

Collagen

Collagen is the major stress resistant material of the dermis and provides a tensile strength to it. It makes up 70%~80% of the dry weight of the dermis. There are many, genetically distinct, collagen proteins, all with triple helical molecules, and are all rich in hydroxyproline and hydroxylysine. Collagen fibers are polymerized by collagen fibril, whose diameter is about 70~140 nm. The main component of skin collagen are type Ⅰ (85%) and Ⅲ (15%).

Elastic fibers

They consist of aggregates of protein filaments and elastin. The amino acids desmosine and isodesmosine are unique to the elastic fibers. The elastic fibers in the papillary dermis are fine while those in the reticular dermis are coarse. They play a major role in maintaining the elasticity of the skin.

Reticulum fibers

Reticulum fibers are the first formed fibers during the embryonic life and in various pathologic conditions associated with increased fibroblastic activity. They are found around the blood vessels and act as basket like capsule around the fat cell.

Ground substance (matrix)

It is an amorphous extracellular material that enmeshes the fibrillar and cellular components of the dermis. It is composed of acid muco-polysaccharides, principally hyaluronic acid, chondroitin sulfate and dermatan sulfate, neutral polysaccharides, and electrolytes.

Vasculature

The dermal vasculature is formed by the superficial and deep plexus. The superficial plexus lies within the papillary dermis. It is parallel to the epidermis and sends capillary end arterioles, and venules to the dermal papillae. The deep plexus is located in the deep reticular dermis, just adjacent to the subcutaneous fat. It is comprised of larger blood vessels. The superficial blood vessels communicate with the deep plexus.

Glomus bodies, specialized aggregates of smooth muscle located between the arterioles and venules, serve to shunt the blood from arterial to the venous side, bypassing the capillaries. They are best developed on the digits. They account for with temperature regulation.

Appendages

The appendages of the skin are constituted by the hair, nails, eccrine and apocrine glands, ducts, and pilosebaceous units.

Eccrine sweat units

These are distributed all over the body except the vermillion border of the lips, nailbeds, labia minora, glans penis, and inner aspect of the prepuce. Their density is maximum on the palms, soles, and axillae. They are composed of the following three components: (i) the secretory portion (ii) the intradermal duct and the (iii) intraepidermal duct. The secretory portion lies at the interface of the dermis and subcutaneous fat. It is composed of one layer of secretory cells surrounded by a layer of flattened myoepithelial cells. The secretory cells are of 2 types, namely the large pale, glycogen rich cells and dark staining, smaller cells. The paler cells initiate the sweat formation while the dark cells modify it by actively reabsorbing sodium. The intradermal eccrine duct is composed of two layers of small, cuboidal, deeply basophilic epithelial cells. The intraepidermal eccrine duct extends from the base of the Rete ridges to the surface. It has a spiral course. It consists of a single layer of inner or luminal cells and two to three layers of outer cells. The secretory portion produces a precursor sweat that is isotonic with plasma. Subsequently, aldosterone acts upon the epithelium lining, the eccrine duct and stimulates resorption of sodium in partial exchange for potassium. However, the duct is relatively impermeable to water. Hence, the sweat that is excreted is hypotonic. It has a specific gravity of 1.005 and the pH is 4.5 to 5.5. It contains sodium, chloride, phosphorus, magnesium, iodide, sulfate, iron, zinc, amino acids, and proteins. The major function of sweat is to dissipate heat by evaporation. One liter of evaporated sweat removes 585 kilocalorie of heat from the body. An increase in body temperature of 0.01℃ excites hypothalamic stimulation of sweating via the different pathway of the sympathetic nervous system.

Apocrine units

Apocrine glands are located in the axillae, areolae, periumbilical, perineal, circumanal areas, prepuce, scrotum, monspubis, labia minora, external ear canal (ceruminous glands) and eyelids (Moll's glands). They are small and nonfunctional till puberty, after which they enlarge. The apocrine gland is composed of (i) a coiled secretory portion located in lower dermis and (ii) a straight excretory portion that empties into the infundibulum of the hair follicles above the sebaceous duct. The secretory portion of apocrine gland is lined by a single layer of pale staining columnar cells. The nuclei of these cells are pushed toward the base. These are the secretory cells. The cell surrounding the secretory cells are: (i) a layer of contractile myoepithelial cells, (ii) PAS: positive basement membrane, and (iii) type Ⅲ collagen and elastic fibers. The excretory duct is composed of two layers of cuboidal cells. Apocrine secretions have no function in men. Bacteria present on the skin surface act upon these secretions to produce short chain fatty acids like ammonia, and other adoriferous substances.

Hair follicles and hair

Hair follicles populate the entire skin surface with the exception of the palms, soles, dorsa of terminal phalanges of the digits,

glans penis, and mucocutaneous junctions. Hair is biologically and morphologically different and distributed in different parts of the body. The fine hair that covers most of the body surface is termed "vellus hair" while the long, coarse, pigmented hair present over the scalp, eyebrows, eyelashes, beard, moustache, axillae, and pubic region are known as "terminal hair". A particular hair follicle may produce different kinds of hair during different stages of life. At puberty, the hair follicles at the axillae, pubic, and beard area start producing terminal hair in contrast to vellus hairs in the prepubertal period.

During embryogenesis, mesenchymal cells in the fetal dermis collect below the basal layer of the epidermis. Epidermal buds grow down into the dermis at these sites. The developing follicle forms at an angle to the skin surface and continues its downward growth. At the base, the column of cells widen and surround the collection of mesenchymal cells forming the hair bulb. The hair is formed from cells just above the bulb. Along one side of the follicle, two buds are formed. The upper one develops into sebaceous gland and the lower one into three segments:(i) the infundibular segment, which extends from the surface opening to the sebaceous duct (ii) the isthmus, which lies between the sebaceous duct and the insertion of arrector pili muscle (iii) the maxtrix, which includes the lower most portion of the hair follicle, that lies below the attachment of arrector pili muscle.

The germinative matrix cells of the hair bulb differentiate along the seven separate pathways forming seven layers. From outwards to inwards, they are:(i) the outer root sheath, (ii) Henle's layer of the inner root sheath (iii) Huxley's layer of the inner root sheath (iv) The cuticle of the inner root sheath (v) the cuticle of the hair shaft (vi) the cortex of the hair shaft (vii) the medulla of the hair shaft.

The growth of the human hair is cyclical. However, each follicle functions as an independent unit and undergoes intermittent stages of activity and quiescence. The growing phase is called "anagen" , during which the cells of the hair bulb actively divide and produce the growing hair. The average duration of anagen is 3 to 10 years. On cessation of this phase, the follicle enters the transitional phase or "catagen". During this phase, the matrix cells stop dividing and the hair develops a brush like zone (club hair). The lower portion of the follicle disappears leaving behind a thin strand of epithelial cells surrounded by a thick basement membrane zone. This phase lasts for 3 to 4 weeks. Next is the resting phase or "telogen". During this phase, the epithelial strand shortens to the level of arrector pili muscle and leaves a small aggregate of epithelial cells exposed to the surrounding dermis. The club hair remains within the shortened follicle until a new anagen hair develops and dislodges it. The telogen lasts for about 3 months.

Sebaceous glands

Sebaceous glands are lipid producing structures that arise as an outgrowth from the upper portion of hair follicles. They are distributed throughout the skin except the palms and soles. They are associated with the hair follicle excluding certain sites, namely the eyelids (meibomian glands), the buccal mucosa and the vermilion border of the lip (Fordyce spots), the prepuce (Tyson glands),

and female areolae (Montgomery tubercles). Microscopically, they are seen to consist of lobules of pale staining, lipid rich cells that are surrounded by an outer layer of cells resembling basal cells, i.e. the germinative cells. The lipid laden cells arise from the germinative cells and gradually disintegrate into an amorphous mass of lipid and cellular debris (sebum); that is, discharged into the sebaceous duct.

Nail units

It is comprised of the nail plate and the tissues around and underneath it. The nail plate is hard, convex, rectangular, and translucent. It is about 0.75 mm in thickness and is situated on the dorsal aspect of the distal phalanx of every finger and toe. It is inserted into the grooves in the skin. The grooves are demarcated by folds of the overhanging skin that form the lateral and proximal nail folds. However, the distal edge of the nail is free. The nail plate rests on the nail bed. The nail bed is comprised of epithelium that overlies a rich vascular dermis. The dermis is contiguous with the periosteum of the distal phalanx. The surfaces of the nail plate and nail bed are firmly attached and it is difficult to separate the two. Distal to the nail bed, is the hyponychium. It is a narrow zone of skin that merges with the palmar skin and the tip of the digit. Finger nails grow at a rate of 0.1 mm daily where as, the toenails grow at a rate of 0.03 mm every day, which is slower.

The nail unit helps in the appreciation of the fine tactile stimuli and also protects the terminal phalanges from trauma. Animals use nails for defense by scratching the opponent's skin with them.

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