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Education

The human hair: from anatomy to physiology

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Abstract

Background Hair is a unique character of mammals and has several functions, from protection of the skin to sexual and social communication. In literature, there are various studies about hair that take into consideration different aspects within many fields of science, including biology, dermatology, cosmetics, forensic sciences, and medicine.

Methods We carried out a search of studies published in PubMed up to 2013.

Results In this review, we summarized the principal anatomical and physiological aspects of the different types of human hair, and we considered the clinical significance of the different structures and the distribution of the hair in the human body.

Conclusion This review could be the basis for improvement and progression in the field of hair research.

Introduction

Hair is a unique character found on all mammals but not on other animals. In humans it is a special and cherished feature, especially in females, but its main functions are in protection of the skin from mechanical insults and to facilitate homeothermy[1,2]; eyebrows and eyelashes, for example, stop things entering the eyes, while scalp hair prevents sunlight, cold, and physical damage to the head and neck.[3] It also has a sensory function, increasing the perception of the skin surface for tactile stimuli, and subserves important roles in sexual and social communication, considering the psychological impact on quality of life seen in hair disorders, such as hirsutism, hair loss, etc.[3,4] In particular, regarding this last point, a significantly higher prevalence of personality disorders in subjects with androgenetic alopecia regarding the prevalence of such diagnoses in the general population have been reported.[5]

Mammalian skin produces hair almost all over the body surface except for a few areas of the body, i.e., sole of the foot, palm of the hand, buccal surface of the lip, and portions of external genitalia; in addition, considering the distribution of human hair in different areas of the body surface, it is possible to note that human hair growth is reduced with tiny and virtually colorless hair on most of the body surface, whereas hair is longer, thicker, and heavily pigmented in other areas, such as the scalp, eyelashes, and eyebrows. Differences are also related to the hair's form, which can be straight, helical, or wavy; color, depending on the balance of different types of melanin (brown to black, indolic eumelanin, and yellow to reddish brown, sulfur-containing pheomelanin); length; diameter; and cross-sectional shape.[3,6,7]

Human hair is usually classified according to three conventional ethnic human subgroups, i.e., African, Asian, and European. Nevertheless, a recent study showed that it is possible to classify the various hairs found worldwide into eight main coherent hair types, by the measurement of three easily accessible parameters: curve diameter; curl index; and number of waves.[8]

Based on different aspects and points of view, several studies on human hair have been made within many fields of science, including biology, dermatology, cosmetics, forensic sciences, and medicine.

The aim of this review is to summarize the principal anatomical and physiological aspects of the different

types of human hair and to consider the clinical significance of the different structures and distribution of hair in the human body.

Anatomy and Physiology of the Hair

Macroscopic and microscopic structures of the hair

Hair is a derivative of the epidermis. Externally, hair is thin, flexible tubes of dead, fully keratinized epithelial cells, whereas inside the skin, it is a part of individual living hair follicles, cylindrical epithelial downgrowths into the dermis, and subcutaneous fat, which enlarge at the base into the hair bulb surrounding the mesenchymal-derived dermal papilla.[3]

From a macrostructural point of view, hair varies in length, diameter, color, and cross-sectional shape among the different ethnic groups and among singular individuals.[9]

Hair has two separate structures: the follicle in the skin and the hair shaft, which is visible on the body surface (Fig. 1).

The hair shaft consists of a cortex and cuticle cells, and in some cases, a medulla in the central region. The medulla is the central part of the hair, whereas the cortex, which represents the majority of the hair fiber composition and plays an important role in the physical and mechanical properties of hair, is the peripheral part and is made up of approximately 50–60% of macrofibrils,

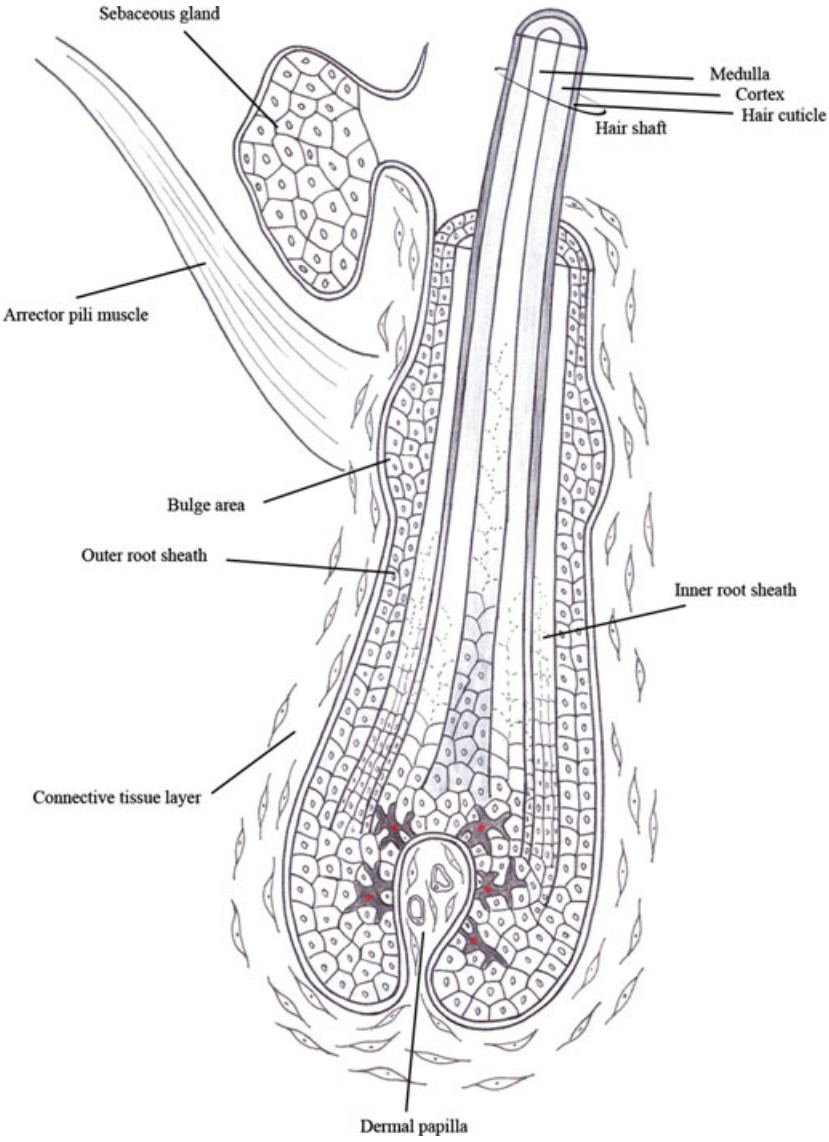

Figure 1 Hair and its follicle. *Melanocytes

which consist of rods of microfibrils embedded into a matrix.[10] The hair shaft cuticle covers the hair from the root to the tip of the epidermis and is formed by flat overlapping cells.[11] Each cuticle cell is generally 0.3–0.5 μm thick, and its visible length is about 50 μm; it consists of various sublamellar structures (the epicuticle, A-layer, exocuticle, endocuticle, and inner layer) and the cell membrane complex.[10] The integrity and properties of the cuticle layer have an important role in protecting the cortex from physical and chemical insults and in maintaining the hair in a clean and disentangled state and have a great impact on its appearance.[12]

The follicle is the essential growth structure of hair. From the outermost aspect of the follicle, the histological structures are:

1 the outer root sheath (ORS), which has been identified as a reservoir of multipotent stem cells, i.e., keratinocyte and melanocyte stem cells, and contains keratinocytes. The ORS forms a distinct bulge area between the insertion of the arrector pili muscle and duct of the sebaceous gland.[3,13] Adjoining the ORS on the dermal side is a basket-like arrangement of two orthogonally arrayed layers of collagen fibers, the glassy layer[14] known as the dermal sheet.[15]
2 the inner root sheath (IRS) consists of three layers: Henle's layer, Huxley's layer, and cuticle layer. The IRS cuticle layer adjoins the cuticle of the hair shaft, anchoring the hair shaft to the follicle. IRS cells produce keratins and trichohyalin that serve as an intracellular cement giving strength to the IRS to support and mold the growing hair shaft, as well as guide its upward movement. The IRS separates the hair shaft from the ORS.[3]

The hair bulb is the portion of the follicle which actively produces the hair. It encloses the follicular dermal papilla, dermal papilla cells, mucopolysaccharide-rich stroma, nerve fibers, and a single capillary loop. The follicular papilla is believed to be one of the most important drivers to instruct the hair follicle to grow and form a particularly sized and pigmented hair shaft; moreover, it is an essential source of growth factors (keratinocyte growth factor, bone morphogenetic protein, hepatocyte growth factor, insulin-like growth factor, stem cell factor), critical for hair growth and melanogenesis.[3,16]

The hair bulb can be divided into two regions: a lower region of undifferentiated cells and an upper region in which the cells became differentiated. A line across the widest part of the papilla separates the two regions at the critical level (Auber's line). Below the Auber's line lies the matrix, or germination center of the follicle, where every cell is mitotically active, and the dermal papilla. From the matrix, cells move to the upper part of the bulb, where they increase in volume and become elongated vertically.[3]

The upper bulb can be divided into four parts: (i) above the critical level, in the wide portion of the bulb, is the pre-elongation region, where the cells align themselves vertically and become slightly larger; (ii) above this region, where the diameter of the bulb is narrower and the cells become conspicuously elongated, is the cellular elongation region; (iii) immediately above, in the cortical pre-keratinization region, distinct fine fibers or fibrils stainable with basic dyes can be seen; and (iv) further up is the keratogenous zone where the cells become hyalinized and the keratin of the hair is stabilized. Depending upon the length of the follicle, the keratogenous zone terminates at approximately one-third of the way between the tip of the papilla and the surface of the skin.

Above the bulb, the upper hair follicle is composed of two anatomical parts: the infundibulum and the isthmus. The infundibulum is a funnel-shaped structure filled with sebum, a product of the sebaceous gland; it extends from the surface of the skin to the sebaceous duct, serves as a reservoir, and provides an interface for interactions with hair follicle-associated cell populations. In detail, in the upper part, called the acroinfundibulum, the epithelium is continuous with the keratinized epidermis and is covered by an intact, rather impermeable stratum corneum; this barrier is interrupted in the lower follicular infrainfundibulum, as the differentiation pattern switches from epidermal differentiation to a tricholemmal differentiation pattern. Only few differentiated corneocytes remain, and the invagination of the epidermis in the infundibulum must be considered as highly permeable.[17]

The isthmus completes the upper part of the hair follicle, and it extends from the duct of the sebaceous gland to the exertion of arrector pili muscle.[3,18]

The innervation and vascularization of a hair follicle

The innervation and vascularization of hair represent an interesting aspect in hair research. In literature, there are data about both, even if the description of the detailed architecture of nerves was more difficult.

Nerves that supply the hair follicles are arranged similarly to the dermal nerve network and include sensory afferents and autonomic sympathetic nerves. Nerves for hair follicles rise from the dermis or subcutaneous tissue and ascend from the dermal network to innervate the hair follicle from the bulb to the epidermis. At the level of the sebaceous gland, some, but not all, hair follicles are surrounded by a collar of nerves, frequently called the hair end organ, which is arranged in an outer circular layer and an inner longitudinal layer. Fibers may extend from this collar to innervate local structures or form a second primarily horizontal dermal plexus located at the junction of the papillary and reticular dermis. Nerve branches extend from this network, primarily in association with

vessels, to innervate the papillary dermis and epidermis.[19] Variations in nerve supply to hair follicles have been reported with respect to the size of the hair.[20]

Similarly, the cutaneous vascularization is provided by arterioles that enter the subcutaneous fat and ascend into the dermis forming a plexus that supplies cutaneous structures such as the hair follicle. These arterioles are concentrated at the lower portion of the hair follicle and form a rich vascular network connected by cross-shunts around the lower one-third of the hair follicle.[19]

During different phases of the hair cycle, some variations are reported. In particular, during anagen there is a substantial increase of perifollicular vascularization correlated with the upregulation of vascular endothelial growth factor expression by keratinocytes of ORS.[3]

Physiology of the hair: hair growth cycle

A hair arises from the integrated activities of several keratinocyte layers in the hair follicle. The development of hair is a dynamic, cyclic process in which the duration of growth cycles is coordinated by many hormones and cytokines and depends not only on where the hair is growing but also on some other factors, such as the individual's age and stage of development, nutritional habits, or environmental alterations like day-length.[10] Important players of this cycle are mainly cytokines (hormones), which are able to instruct the follicle to undergo appropriate changes, so that each hair can be in a different stage of growth cycle compared to the adjacent hairs.[21–23]

Hair follicles grow in repeated cycles, in which stages of rapid growth and hair shaft formation alternate with stages of apoptosis-driven hair follicle regression and relative hair follicle quiescence.[24,25] In particular, the hair growth cycle can be divided into three distinct phases: (i) anagen or growth phase; (ii) catagen or transitional phase; and (iii) telogen or resting phase (Fig. 2).

The anagen phase is an active growth phase, during which the hair follicle enlarges reaching its characteristic onion shape and a hair fiber is produced. It can be divided into six stages (I–VI). During anagen I–V (proanagen), hair progenitor cells proliferate, envelope the growing dermal papilla, grow downwards into the skin, and begin to differentiate into the hair shaft and IRS; then, the newly formed hair shaft begins to develop and the melanocytes located in the hair matrix show pigment-producing activity; in anagen VI (metanagen), full restoration of the hair fiber-producing unit is realized, which is characterized by formation of the epithelial hair bulb surrounding the dermal papilla, located deep in the subcutaneous tissue, and the new hair shaft appears from the skin surface. This phase can last for several years in hair follicles.[3,26]

The catagen phase starts when the anagen growth phase comes to the end. At the beginning of the catagen phase, differentiation and proliferation of hair matrix keratinocytes decreases significantly, the pigment-producing activity of melanocytes stops, and hair shaft production is completed. The hair follicle undergoes apoptosis-driven regression resulting in a reduction of about one-sixth of the normal diameter. During catagen, a specialized structure, the club hair, is formed. The keratinized brush-like structure at the base of the club hair is surrounded by

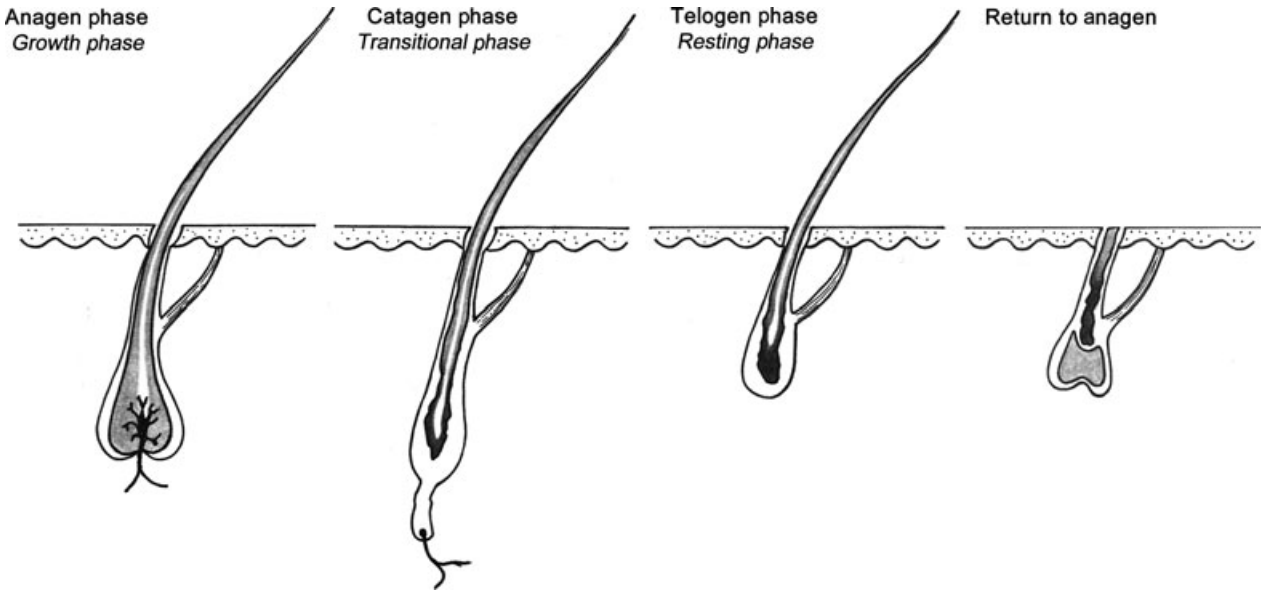

Figure 2 Different phases of hair cycle

epithelial cells of the ORS and anchors the hair in the telogen follicle. The dermal papilla is transformed into a cluster of quiescent cells closely adjacent to the regressing hair follicle epithelium and travels from the subcutis to the dermis/subcutis border to maintain contact with the distal portion of the hair follicle epithelium, including the secondary hair germ and the bulge. This phase lasts for a few weeks.[3]

The telogen phase begins after the catagen phase; the hair goes into a resting phase, and this period can last few weeks (eyelashes) to eight months (scalp hair). Although the hair does not grow during this stage, the dermal papilla stays in the resting phase. Telogen hair follicles are characterized by a lack of pigment-producing melanocytes and the IRS. Their dermal papilla is closely attached to a small cap of secondary hair germ keratinocytes containing hair follicle stem cells. Approximately 10–15% of all hairs are in resting phase at any given moment.[3] At the end of this stage, the hair falls (exogen phase); a few weeks later, the hair follicle re-enters the growth phase by stimulating stem cells from the bulge area.[18]

Follicular stem cells as well as a strict interaction between epithelial, mesenchymal, and melanocytic cells are necessary for maintaining and regulating the hair cycle. The hair follicle bulge area stem cells may provide an accessible source of undifferentiated multipotent stem cells critical for hair follicle development and function, including hair follicle pigmentation.[23]

In particular, the bulge activation theory proposes that factors in the papilla act on the stem cells of the bulge region to modulate the cycle. According to this theory, stem cells in the bulge region start to proliferate after responding to signals from the dermal papilla; bulge cell proliferation is the cellular source of the entire hair follicle structure, including the hair matrix and matrix cells; these cells are transient amplifying cells, which can undergo only a limited number of mitoses, thus establishing the length of anagen and the onset of catagen; then, the upward movement of the follicular papilla during catagen is crucial for re-establishment of follicular–papilla–bulge cell contact and the induction of a new hair cycle.[27–29]

Knowledge of the mechanism of hair cycle is essential for understanding hair growth disorders. In particular, anagen–catagen transformation is important for this aspect; therefore, the ability to accurately and sensitively recognize the anagen–catagen transformation is fundamental for hair research. Regarding this, Kloepper and colleagues[25] have provided a method to objectively distinguish between anagen and catagen in human hair follicle organ culture; in particular, they suggested seven qualitative criteria based on assessing the morphology of hair matrix, dermal papilla, and the distribution of pigmentary markers, and 10 quantitative criteria based on the morphometric evaluation of cell number, proliferation, apoptosis, and hair follicle pigmentary markers. However, they also underline that organ culture human hair follicles do not show the complete, classic sequence of catagen transformation *in vivo*, but catagen transition *in vitro* develops much faster and sooner or later is overshadowed by hair follicle degeneration before catagen transformation has been completed.

Molecular Structure of the Hair

As previously reported, hair is a keratinized structure. It is enclosed by the cuticle and contains about 100 cells mutually separated by the cell membrane complex. The hair cells in the cortex are mainly constituted by macrofibrils (90%) and nuclear remnants and pigment granules (10%). In turn, one macrofibril is composed of a few hundred filament proteins densely packed in a less-ordered matrix. The filaments of $\approx$ 8 nm in diameter are generally less polar, contain less cysteine, and are larger than the matrix proteins of $\approx$ 2 nm.[30]

From a molecular point of view, the major proteins synthesized in the hair shaft are alpha-keratin intermediate filaments and keratin-associated proteins (KAP; high/ultrahigh cysteine and high glycine–tyrosine) essential for the formation of rigid and resistant hair shafts through their extensive disulfide bond cross-linking with the abundant cysteine residue of hair keratins or hydrophobic interactions with keratins.[31]

The alpha-keratin genes enclose 54 functional genes (28 type I genes and 26 type II genes) that are clustered on chromosomes 12q13.13 and 17q21.2 that show different expression patterns during hair development.[32] Among the 28 type I genes, 11 genes encode type I hair keratins; similarly, of the 26 type II genes, six encode hair keratins. Hair keratin forms the intermediate filament network by copolymerization of type I and II members.[33]

The KAP that constitutes the matrix of the keratin is a large group of up to 100 different proteins. The matrix proteins fall into three main families according to their amino acid composition and molecular size; they are designated as the high-sulfur proteins, the ultra-high sulfur proteins, and the high-glycine–tyrosine proteins. The high-sulfur proteins arise predominantly from the cortex (KAP1, 2, 3, 13, 15, and 23), but some have their origins in the cuticle (KAP13 and 23) and the matrix (KAP11 and 13). The ultra-high sulfur proteins (KAP4, 5, 9, 10, 12, and 17) and the high-glycine–tyrosine proteins (KAP6–8 and 19–21) likewise occur in the cortex (KAP6, 7, 19, 20, and 21), the cuticle (KAP19), and the matrix (KAP8).[34,35]

Immunology of the Hair Follicle

A few well-defined tissue compartments in the mammalian body are immunologically privileged. These sites include the anterior eye chamber, parts of the testis and ovary, the adrenal cortex, segment of the central nervous system behind the blood–brain barrier, the fetomaternal placental unit, hamster cheek pouch, and probably the proximal nail matrix.[36]

The term immune privilege (IP) was created by Sir Peter Medawar in 1948 to describe the protection of vital structures from the potentially damaging effects of an inflammatory immune response after inoculation of allotransplants into certain organs such as the brain.[37] This definition was then extended to tissue sites in which a number of mechanisms collaborate to suppress a cytokine immune attack on the cells and antigens harbored within these sites.

A collapse of the IP leads to unrestricted immune-mediated inflammation and has devastating consequences for the individual. For example, in the brain or eye, a collapse of IP may result in neurodegeneration or loss of vision[38]; even loss of IP at the maternal–fetal interface during pregnancy may result in fetal loss and, analogously, IP failure in testis would result in male infertility.[39,40] In addition, other organs and tissues permanently exposed to potentially deleterious foreign antigens and with large epithelial surface are also included in this local immunosuppressive mechanism, such as the gut, vagina, lung, and skin and its appendages.[41]

The IP concept reflects a complex immune network of interacting immunoregulatory process and immunosuppressive microenvironments. In particular, it is established and maintained by:

1 lack or low expression of classical major histocompatibility complex (MHC) class Ia expression, which sequesters autoantigens in tissue sites and hinders their presentation to CD8 + T cells with a matching T-cell receptor;
2 human leukocyte antigen molecules are present and probably involved in the inhibition of T-cell proliferation and in the downregulation of natural killer cell responses;
3 local production of potent immunosuppressants such as transforming growth factor β, α-melanocyte-stimulating hormone (α-MSH), interleukin-10, and others.
4 functional impairment of antigen-presenting cells;
5 absence of lymphatics;
6 establishment of extracellular matrix barriers to hinder immune cell trafficking;
7 expression of nonclassic MHC class Ib molecules; and
8 expression of Fas ligand to delete autoreactive Fas-expressing T cells.

The human hair follicle appears to represent a specialized compartment of the skin immune system and, consequently, it qualifies as an IP site.[22,42] The immunology of hair is very intriguing and complicated. This miniorgan is unique among all other IP sites, which is distributed over the human body and consequently is highly accessible to experimental analysis and manipulation. Although there are phenomenological indications, rejection and survival of heterologous tissue transplants within this tiny miniorgan have not yet been studied. The only available evidence that hair follicles can shelter heterotransplants from immuno-rejection was provided by Billingham and Silvers,[43] who provided a special milieu that permits transplanted allogenic cells to escape limitation by the host immune system. They observed that, while donor melanocytes within the epidermis are rapidly removed, heterologous epidermal melanocytes show long-term survival if they manage to escape into the anagen hair bulb of (white) host guinea pigs, which thus began to produce black hair shaft.[43,44] Other evidence was not reported until the study of rat hair follicle MHC class I expression[45]; even evidence about IP in the human anagen hair bulb were then reported.[22,38] In particular, the main key features of IP in the anagen hair bulb are: absence or very low level of MHC class I expression in the proximal epithelium and melanocytes; relative MHC Ia negativity of the anagen hair bulb correlates well with a downregulation of the MHC class I pathway-related molecules α-microglobulin and transporter of antigen processing-2; expression of potent immunosuppressants, such as transforming growth factor β1, adrenocorticotropin hormone (ACTH), and α-MSH; greatly reduced number of antigen-presenting cells, which appear to be functionally impaired because they do not express MHC class II antigens; absence of intraepithelial T cells; absence of lymphatics and presence of a special extracellular matrix barrier which may combine to hinder immune cell trafficking.[22] Moreover, the hair follicle's stem cell zone, the bulge, even expresses non-classic MHC class I molecules (MHC class Ib molecules), which inhibit, for example, natural killer cell activities and express potent immunosuppressants.[36]

However, what is the function of hair follicle IP? Hair follicle IP is generated and maintained during each anagen phase to sequester potentially deleterious, anagen- and/or melanogenesis-associated autoantigens from immune recognition by appropriately sensitized Cd8 + T cells with cognate receptors, primarily via downregulation of MHC class I and by the local production and secretion of potent immunosuppressants.[22] In particular, the hair follicle epithelium rhythmically generates, maintains, and deconstructs an area of relative IP in the hair follicle, which is present only during a defined segment of

the hair cycle, which is the anagen phase and absent during hair follicle regression (catagen) and in the resting phase (telogen). In contrast, the bulge area continuously seems to enjoy a relative IP.[36]

There are compelling clinical and biological reasons for systemic characterization of the hair follicle immune system in diseases. Abnormalities or dysfunction of the hair follicle immune system, in fact, can explain the very high incidence of folliculitis in immunocompromised patients and that a collapse of hair follicle and/or bulge area IP is of critical importance in alopecia areata (AA), lichen planopilaris, and cicatricial alopecia.[22,36,46–49]

Classification of the Hair

Humans have several different types of hair that can be classified depending on their body position and form. Moreover, size, angle of penetrance through the skin, embryological time of first appearance, and structural variations in the hair follicles (hair follicle density, size of follicular orifices, hair shaft diameter, volume, and surface of the infundibula) are all taken into account when classifying hair types. Hair shaft diameters show relatively little variation (16–42 μm); the highest shaft diameter is observed in the sural (42 μm) and thigh (29 μm) regions, with the lowest in the forehead (16 μm). The highest average hair follicle density is found on the forehead (292 follicles/cm^2). The highest follicular infundibula volume, which is interpreted as a potential follicular reservoir for dermally applied substances, is on the forehead (0.19 mm^3/cm^2) as well as in the sural region (0.18 mm^3/cm^2).[50]

Furthermore, the cycle's length varies on different parts of the body. For eyebrows, the cycle is completed in about four months, while it takes the scalp 3–4 years to finish.

Types of hair follicles

Human hair could be classified as (i) androgen-independent hair (i.e., eyebrows and lashes); and (ii) hair on hormone-dependent body regions (i.e., scalp, beard, chest, axilla, and pubic region), which consist of terminal hair shafts, which are long (>2 cm), thick (>60 mm in diameter), pigmented, and medullated.[45] The medulla is located in the large terminal hair fibers, but most scalp hair is not medullated. Terminal hair usually extends more than 3 mm into the hypodermis.

The rest of the body in adults is covered with vellus hair (androgen-independent hair) – short (<2 cm), thin (<30 mm in diameter), often unpigmented, and extending just 1 mm into the dermis.

Some hair follicles, cited as intermediate hair, can exist in a transitional phase between terminal and vellus forms.[18,51,52]

Type of hair

In the literature, there are some data about features of the different types of hair. However, major documents concern the scalp, pubic, and axillary hair, and hair in the phalanges; no studies about the comparison among the structures of the different types of hair are reported. For this reason, in the next paragraphs we have summarized only the main features of the most considered hair types.

Scalp hair

In the scalp, the hair follicles are typically arranged in the follicular unit composed of one to four terminal hairs and one to two vellus hairs, sebaceous gland, and encircled by the same arrector pili muscle. Each hair grows steadily, approximately 1 cm per month and continuously for 3–5 years (anagen phase). Growth then stops and is followed by a brief catagen phase and a 2–4-month telogen phase, during which old hair is shed. With the onset of the anagen phase, new hair starts to grow from the same follicle.

Scalp hair is a fiber 60–80 μm in diameter, and its exterior consists of a layer of flat, imbricated scales pointing outward from root to tip.[10]

The dimensions of the scalp hair follicle are well documented in morphometric analysis. The total length of the follicle and the length of the infundibulum differ significantly in terminal (3864 ± 605 μm) and vellus hair follicles (580 ± 84 μm). Furthermore, the diameter of the terminal hair follicle opening on the skin surface level is twice as large as that of the vellus hair follicle. The thickness of the epithelial lining is significantly lower in vellus hair follicles (45 ± 14 μm) as compared to terminal hair follicles (65 ± 20 μm).[17]

Disorders of the scalp often result in severe pathologic and cosmetic interference with skin disease and quality of life, creating the need for optimal medical surveillance.

Pubic and axillary hair

Pubic and axillary hair development signals puberty in both sexes. Pubic hair is the hair in the frontal genital area of adolescent and adult humans, located on and around the sex organs, the crotch, and sometimes at the top of the inside of the legs. Although fine vellus hair is present in the area in childhood, pubic hair is considered to be the heavier, longer, and coarser hair that develops during puberty as an effect of rising levels of androgens. Pubic hair changes with hormonal diseases and reduces with age (typically after menopause in women).

A recent paper by Mistry and colleagues[53] reported the variations among the scalp, pubic, and axillary hair. Apart from its length and its natural color, hair displays a morphological diversity both macroscopically and

microscopically. Examination on incidence of medullation revealed a significantly higher absence of medullation in scalp hair in comparison with axillary and pubic hair. The quantitative variables in the different hair types revealed significantly higher shaft diameters in pubic hair compared to that of axillary and scalp hair. However, the shaft diameter of scalp hair demonstrated a general trend of higher value than that of axillary hair. The medulla diameter was also found to be significantly higher in pubic hair compared to that of scalp and axillary hair.

Phalangeal hair

Phalangeal hair is concentrated in a particular region of the phalanx and is different from hair on other parts of the body; moreover, their distribution may be influenced by some factors such as genes and environment.

The distribution of phalangeal hairs was studied in a sample population of Nigerian Yorubas. The highest percentage of hair distribution was observed in the proximal phalanges and in males; in addition, their number was greater on the left than on the right, probably because more people use the right hand than the left. The presence is also affected by job type (a higher number was observed in office workers than in field workers), whereas no difference was found to be related to age, although teenagers and older people appeared to have a higher percentage of hair than adolescents. Regarding the distribution of hairs, the proximal phalanges have the highest percentage, whereas middle phalangeal hairs are not common and distal phalanges are rare.[6]

A study conducted by Egesi and Rashid[54] examined the presence of middle phalangeal hairs in relation to their presentation (is mostly on the fourth finger), age (the highest incidence was in the 10–15-year-old age group and gradually decreased to a maximum at age 35), race (Caucasians had a higher incidence than other ethnic groups), sex (women had less occurrence of middle phalangeal hair compared to men), and use as an identifiable marker for medical significance in certain medications.

Clinical Observations on the Human Hair

Hormone and hair follicles

The effects of neurohormones on hair follicle growth are very complex and strongly dependent of hair cycle stage. A close localization of sensory and autonomic nerve fibers and bulge area support the possibility that neuropeptides and neurotransmitters may influence stem cells and modulate hair cycle. However, it is now clear that human hair follicles are not only a target of neuromediators, but they are also a non-classic production site for neurohormones, which are synthesized by keratinocytes, melanocytes, and fibroblasts.[55]

Several studies in humans showed the expression of a neuroendocrine system in the human hair follicle.[56,57] In particular, the expression of corticotropin-releasing hormone (CRH), urocortin, and CRH receptors, the propiomelanocortin-derived neuropeptides (α-MSH, β-endorphin, ACTH, thyrotropin-releasing hormone, melatonin) and their associated receptors, has been previously reported.[58,59]

The role of neurohormones and neuropeptides in human hair follicle pigmentation extends far beyond the control of melanin synthesis by α-MSH and ACTH and includes melanoblast differentiation, reactive oxygen species scavenging, maintenance of hair follicle IP, and remodeling of the hair follicle pigmentary unit.[55]

There are several clinical evidences about the involvement of neurohormones in hair pathologies. In humans, an overproduction of ACTH is a well-recognized cause of acquired hypertrichosis, which is a process in which non-pigmented vellus hair follicles are converted into large terminal hair follicles with a strong and pigmented hair shaft. This induction of hypertrichosis by ACTH suggests evidence that the neuropeptide may stimulate and/or prolong the anagen phase.[56]

Other data suggest that severe psycho-emotional stress may cause the onset of AA. This effect may be mediated by CRH release that acts as a direct proinflammatory peptide or through activation of mast cells leading to the destruction of the hair root.[60] More recently, another study confirmed the enhanced expression of CRH, ACTH, and α-MSH in AA.[61]

Aging

Aging is associated with progressive decreases in the maximal function and reserve capacity of all organs in the body, including the skin. The most common phenomenon of aging in hair is graying. It occurs in the fourth decade regardless of gender, even if some clinical differences are noted between men and women: the temporal and occipital area are more involved in men than in women and, usually, graying starts in the temporal area in men and in the frontal area in women.[62] Maintenance of hair pigmentation is dependent on the presence and function of melanocytes, which are maintained by the stem cells of the bulge area of the hair follicle. Loss of melanocytes and melanocyte stem cells is associated with the loss of hair pigmentation seen with human aging. In particular, studies for pMel17 and microphthalmia-associated transcription factor demonstrated a decreasing number of unpigmented melanocytes in the bulge region of the hair follicle.[63] In addition, recent data suggest a complete depletion both of mature melanocytes and of immature melanoblasts in aged hair follicles, which results in melanocyte stem cell depletion and subsequent hair graying.[64]

Advancing age is also accompanied by a decrease in the number of hair follicles on the body and scalp and an increase in the proportion of telogen hair follicles. In some areas, such as the face, hormone modification can improve the number of hairs or change their shape (there is more curling of temporal hair in men). The remaining hairs may be smaller in diameter and may grow more slowly. The effect of aging on hair diameter and surface features was recently investigated in a Korean population, using atomic force microscopy, showing that hair diameter increased for the first 20–30 years of life, after which it began to decrease, whereas the surface roughness increased significantly with age.[65]

Diagnostic use

Hair shaft can be used for diagnostic purpose and, in particular, for testing psychoactive drugs[9] and for determining the concentration of metals in relation to sex and age, such as poisoning (lead).[66] Moreover, the condition of hair cuticles has the potential to assist in the diagnosis of health disorders and can be used forensically to provide information on the identity and lifestyle of the hair's owner.[11]

Conclusions

As reported in this review, there are several aspects regarding human hair that should be taken into consideration to obtain increasingly more results in different fields, including biology, dermatology, cosmetics, forensic sciences, and medicine. Here, we reported and summarized the main aspects of the anatomy and physiology of human hair for providing a useful overview that could be the basis for the improvement and progress in the field of hair research.

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