3

The Microscopic Structure of the Epidermis and Its Derivatives

Joel J. Elias
University of California at San Francisco School of Medicine, San Francisco, California

A general review of the microscopic structure of the epidermis and those epidermal derivatives that are distributed widely over the skin and, therefore, may be of interest in considerations of mechanisms of percutaneous absorption, will be presented here. Both light and electron microscopic information will be discussed in order to give an integrated brief summary of the basic morphological picture.

The epithelial component of the skin, the epidermis, is classified histologically as a stratified squamous keratinizing epithelium. It is thickest on the palms and soles (Fig. 1) and thinner elsewhere on the body (Fig. 2). It lies on the connective tissue component of the skin, the dermis, in which are located the blood vessels and lymphatic vessels. Capillary loops in the dermis come to lie in close apposition to the underside of the epidermis. The epidermis, in common with other epithelia, is avascular. The living cells of the epidermis receive their nutrients by diffusion of substances from the underlying dermal capillaries through the basement membrane and then into the epithelium. Metabolic products of the cells enter the circulation by diffusion in the opposite direction.

As in the case of other epithelia, the epidermis lies on a basement membrane (basal lamina). This extracellular membrane, interposed between the basal cells of the epidermis and the connective tissue of the dermis, serves the important function of attaching the two tissues to each other. The point of contact of the epidermis with this structure is the basal cell membrane of the basal cells. Along this surface the basal cells show many hemidesmosomes, which increase the adherence of the basal cells (and therefore of the entire epidermis) to the basement membrane (and therefore to the dermis). In some locations, such as the renal glomerulus, the basal lamina has been shown to also play a role as a diffusion barrier to certain molecules.

The plane of contact between the epidermis and dermis is not straight but is an undulating surface, more so in some locations than others. Upward projections of connective tissue, the dermal papillae, alternate with complementary downgrowths of the epider-

This chapter is reproduced with permission from Bronaugh RL, Maibach HI, eds. Percutaneous Absorption: Mechanisms—Methodology—Drug Delivery. 2nd ed. New York: Marcel Dekker, Inc., 1989.

Marcel Dekker, Inc.
270 Madison Avenue, New York, New York 10016

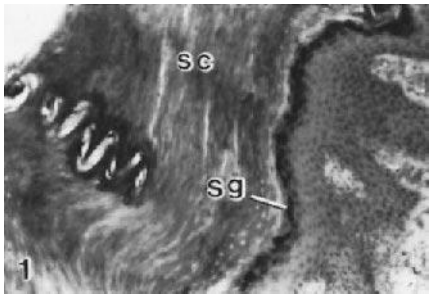

FIGURE 1 Thick epidermis from sole. The spiral channel through the extremely thick stratum corneum (sc) carries the secretion of a sweat gland to the surface. The stratum granulosum (sg) stands out clearly because its cells are filled with keratohyalin granules that stain intensely with hematoxylin. Hematoxylin and eosin. ×100.

mis. This serves to increase the surface area of contact between the two and presumably, therefore, the attachment.

Within the epidermis are found four different cell types with different functions and embryologic origins: keratinocytes, melanocytes, Langerhans cells, and Merkel cells. These will be considered in turn.

The keratinocytes are derived from the embryonic surface ectoderm and differentiate into the stratified epithelium. Dead cells are constantly sloughed from the upper surface of the epidermis and are replaced by new cells being generated from the deep layers. It is generally considered that the basal layer is the major source of cell renewal in the epidermis. Lavker and Sun (1982) distinguish two types of basal cells, a stem cell type and a type that helps anchor the epidermis to the dermis, and an actively dividing suprabasal cell population. The basal cells have desmosomes connecting them to surrounding cells and, as mentioned earlier, hemidesmosomes along the basal lamina surface. They have tonofilaments coursing through the cytoplasm and coming into close apposition to the desmosomes. These protein filaments are of the intermediate filament class and are made up principally of keratin. Basal cells have the usual cell organelles and free ribosomes, the site of synthesis of intracytoplasmic proteins.

As a result of the proliferation of cells from the deeper layers the cells move upward through the epidermis toward the surface. As they do, they undergo differentiative changes

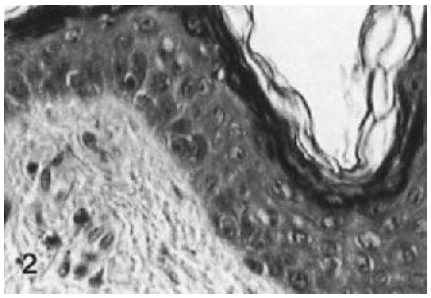

FIGURE 2 Thin epidermis. The strata spinosum, granulosum, and corneum are considerably thinner than in Figure 1. Hematoxylin and eosin. ×200.

which allowed microscopists to define various layers. The cells from the basal layer enter the stratum spinosum, a layer whose thickness varies according to the total thickness of the epidermis. The layer derives its name from the fact that, with light microscopic methods, the surface of the cell is studded with many spiny projections. These meet similar projections from adjacent cells and the structure was called an intercellular bridge by early light microscopists (Fig. 3). Electron microscopy showed that the so-called ''intercellular bridges'' were really desmosomes, and the light microscopic appearance is an indication of how tightly the cells are held to each other at these points. The number of tonofilaments increases in the spinous cells (prickle cells) and they aggregate into coarse bundles—the tonofibrils—which were recognizable to light microscopists using special stains.

Electron microscopy reveals the formation within the spinous cells of a specific secretory granule. These small, membrane-bound granules form from the Golgi apparatus and are the membrane-coating granules (MCG; lamellar bodies; Odland bodies). They contain lipids of varying types which have become increasingly characterized chemically (Grayson and Elias, 1982; Wertz and Downing, 1982).

As the cells of the stratum spinosum migrate into the next layer there appear in their cytoplasm large numbers of granules that stain intensely with hematoxylin. These are the keratohyalin granules and their presence characterizes the stratum granulosum. Electron microscopy shows that the granules are not membrane bound but are free in the cytoplasm. Histidine-rich proteins (Murozuka et al., 1979; Lynley and Dale, 1983) have been identified in the granules. The tonofilaments come to lie in close relationship to the keratohyalin granules. The membrane-coating granules are mainly in the upper part of the granular cell.

When observed by either light or electron microscopy there is an abrupt transformation of the granular cell to the cornified cell with a loss of cell organelles. In thick epidermis, the first cornified cells stain more intensely with eosin and this layer has been called the stratum lucidum. The interior of the cornified cell consists of the keratin filaments, which appear pale in the usual electron microscopic preparations, and interposed between them a dark osmiophilic material. The interfilamentous matrix material has been shown to have derivations from the keratohyalin granule and is thought to serve the function of aggregation of the keratin filaments in the cornified cell (Murozuka et al., 1979; Lynley and Dale, 1983).

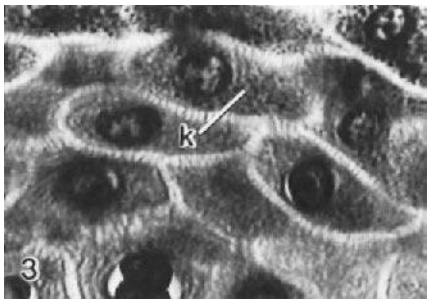

FIGURE 3 High power view of upper part of stratum spinosum and lower part of stratum granulosum. Note the many ''intercellular bridges'' (desmosomes) running between the cells, giving them a spiny appearance. When the cells move up into the stratum granulosum, keratohyalin granules (k) appear in their cytoplasm. Hematoxylin and eosin. ×1000.

In the uppermost cells of the granular layer the membrane-coating granules move toward the cell surface, their membrane fuses with the cell membrane and their lipid contents are discharged into the intercellular space. Thus, the intercellular space in the cornified layer is filled with lipid material which is generally thought to be the principal water permeability barrier of the epidermis (Grayson and Elias, 1982; Wertz and Downing, 1982). The stratum corneum has been compared to a brick wall, with the bricks representing the cornified cells, surrounded completely by mortar, representing the MCG material (Elias, 1984).

The cornified cell is further strengthened by the addition of protein to the inner surface of the cell membrane. Two proteins that have been identified in this process are involucrin (Banks-Schlegel and Green, 1981; Simon and Green, 1984) and keratolinin (Zettergren et al., 1984). A transglutaminase cross-linking of the soluble proteins results in their fusion to the inner cell membrane to form the tough outer cell envelope of the cornified cell. Desmosomes between the cells persist in the cornified layer.

It can be seen that formation of an outer structure (stratum corneum) which can resist abrasion from the outside world and serve as a water barrier for a land-dwelling animal has proven incompatible with the properties of living cells. The living epidermal cells, therefore, die by an extremely specialized differentiative process that results in their non-living remains having the properties that made life on land a successful venture for vertebrates.

Distributed among the keratinocytes of the basal layer are cells of a different embryologic origin and function, the melanocytes. In the embryo, cells of the neural crest migrate from their site of origin to the various parts of the skin and take up a position in the basal layer of the epidermis. They differentiate into melanocytes and extend long cytoplasmic processes between the keratinocytes in the deep layers of the epidermis. Because they contain the enzyme tyrosinase they are able to convert tyrosine to dihydroxyphenylalanine (dopa) and the latter to dopaquinone with the subsequent formation of the pigmented polymer melanin. The tyrosinase is synthesized in the rough endoplasmic reticulum and transferred to the Golgi body. From the latter organelle, vesicles with an internal periodic structure are formed which contain the tyrosinase. These are the melanosomes, the melanin-synthesizing apparatus of the cell. Melanin is formed within the melanosome, and as it accumulates the internal structure of the melanosome becomes obscured. Seen with the light microscope the pigmented melanosome appears as the small brown melanin granule. The melanin granules are then transferred from the melanocyte's cytoplasmic extensions to the keratinocytes, and become especially prominent in the basal keratinocyte's cytoplasm. In this position their ability to absorb ultraviolet radiation has a maximal effect in protecting the proliferating basal cell's DNA from the mutagenic effects of this radiation. Within the keratinocyte varying numbers of melanosomes are often contained within a single membrane-bound vesicle. The classic method of demonstrating melanocytes is the dopa test. Sections of skin are placed in a solution of dopa and only the melanocytes turn a dark brown color (Fig. 4).

Within the epidermis is another population of cells which were first demonstrated by Langerhans in 1868. By placing skin in a solution of gold chloride he showed that a number of cells in the epidermis, particularly in the stratum spinosum, turned black. The cytoplasmic extensions of the cell give them a dendritic appearance. For many decades the nature of this cell type was unknown, including whether it was a living, dead, or dying cell. Electron microscopy showed that it was a viable cell in appearance, lacked desmosomes, and possessed a very unusual cytoplasmic structure—the Birbeck granule.

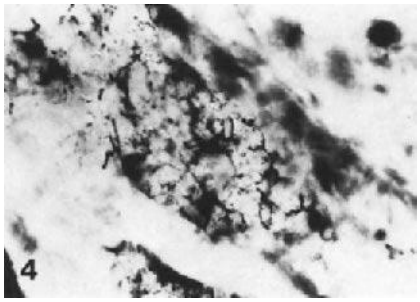

FIGURE 4 A thick section of the epidermis was made with the plane of section running parallel to the surface of the skin and including the deep layers of the epidermis. Dopa reaction shows whole melanocytes on surface view, illustrating their branching, dendritic nature. ×340.

With the development of methods for identifying cell membrane receptors and markers in immune system cells it was shown that Langerhans cells originate in the bone marrow. They are now thought to be derived from circulating blood monocytes, with which they share common marker characteristics. The monocytes migrate into the epidermis and differentiate into Langerhans cells. Considerable evidence shows that these dendritic cells capture cutaneous antigens and present them to lymphocytes in the initiation of an immune response. Their population in the epidermis is apparently constantly replenished by the bloodborne monocytes.

Finally, a fourth cell type, the Merkel cell, can be found in the epidermis. These appear to be epithelial cells and are found in the basal layer. A characteristic feature is the presence of many small, dense granules in their cytoplasm. Sensory nerve endings form expanded terminations in close apposition to the surface of Merkel cells.

Hair follicles begin their formation as a downgrowth of cells from the surface epidermis into the underlying connective tissue. The growth extends into the deep dermis and subcutaneous tissue and forms in the deepest part of the structure a mass of proliferative cells—the hair matrix. The cells of the outermost part of the hair follicle, the external root sheath, are continuous with the surface epidermis. The deepest part of the hair follicle is indented by a connective tissue structure, the hair papilla, which brings blood vessels close to the actively dividing hair matrix cells (Fig. 5). As the cells in the matrix divide the new cells are pushed upward toward the surface. Those moving up the center of the hair follicle will differentiate into the hair itself. The structure of the hair, from the center to the outer surface, consists of the medulla (when present), the cortex and the cuticle of the hair. The cortex forms the major part of the hair. These cells accumulate keratin to a very high degree. They do not die abruptly as in the case of the surface epidermis. Instead, the nucleus of the cell gradually becomes denser and more pyknotic and eventually disappears. Keratohyalin granules are not seen with the light microscope. Cells moving up from the matrix in the region between the hair and the external root sheath form the internal root sheath. Here, the cells adjacent to the hair form the cuticle of the internal root sheath. Next is Huxley's layer and, adjacent to the external root sheath, Henle's layer. These cells accumulate conspicuous trichohyalin granules in their cytoplasm in the deeper part of the internal root sheath. The cells of the internal root sheath disintegrate higher up in the hair follicle and disappear at about the level of the sebaceous gland. Thereafter, the hair is found in the central space of the hair follicle without a surrounding internal root sheath.

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016

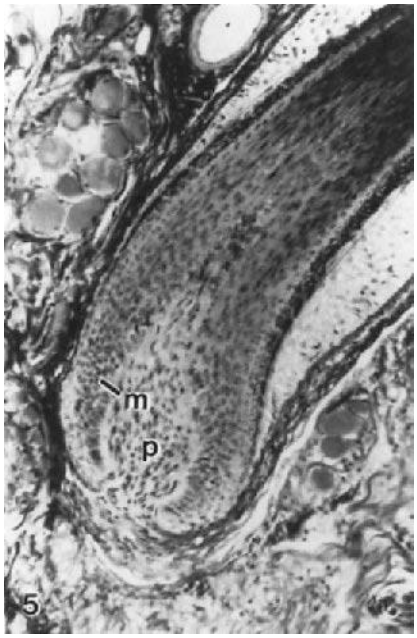

FIGURE 5 The connective tissue hair papilla (p) indents into the base of the hair follicle. The follicle cells in the hair matrix region (m) show many mitotic figures. Iron hematoxylin and aniline blue. ×150.

When viewed with the light microscope the hair follicle is surrounded by an exceedingly thick basement membrane called the glassy membrane. Scattered among the keratinocytes in the hair matrix are melanocytes which transfer pigment to the forming hair cells and give the hair color. Hair growth is cyclic, with each follicle having alternating periods of growth and rest.

About a third of the way down the hair follicle from the surface epidermis, the sebaceous glands connect to the hair follicle. The sebaceous alveoli consist of a rounded, solid mass of epithelial cells surrounded by a basement membrane. The outer cells proliferate and the newly formed cells are pushed into the interior of the sebaceous alveolus. As they move in this direction they accumulate a complex of lipids and lipidlike substances. As the lipids fill the cell it begins to die and the nucleus becomes more and more pyknotic. The cells eventually disintegrate, releasing their oily contents by way of a short duct into the space of the hair follicle (Fig. 6). This is the classic example of holocrine secretion where the entire gland cell becomes the secretion. In some scattered locations (e.g., nipple) sebaceous glands can be found independent of the hair follicle. In other areas their size relative to the hair follicle is very large (Fig. 7). Because the lipids are extracted in the usual histologic preparations the cells typically appear very pale.

The major type of sweat gland in the human, the eccrine sweat gland, is distributed over practically all parts of the body. It produces a watery secretion which is conveyed to the surface of the skin where its evaporation plays an important thermoregulatory role. The eccrine glands arise as tubular downgrowths from the surface epidermis independent of hair follicles. The tubule extends deep into the dermis or the subcutaneous tissue level where it becomes coiled. The eccrine gland, therefore, is a simple coiled tubular gland.

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016

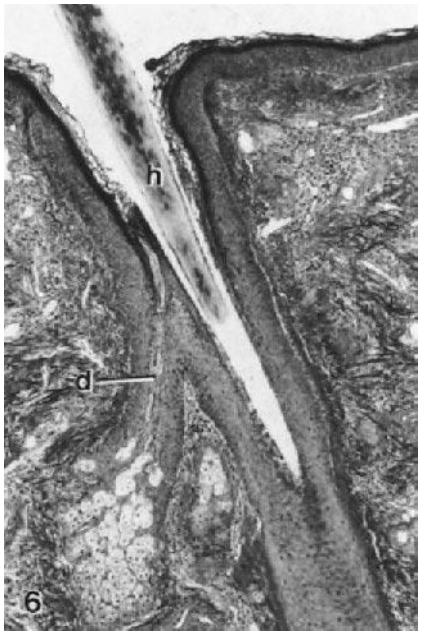

FIGURE 6 Upper part of hair follicle. The hair (h) is shown emerging from the follicle (the lower part of the hair passed out of the plane of section). The sebaceous gland is shown emptying its secretion by way of the duct (d) into the space of the follicle. Iron hematoxylin and aniline blue. ×50.

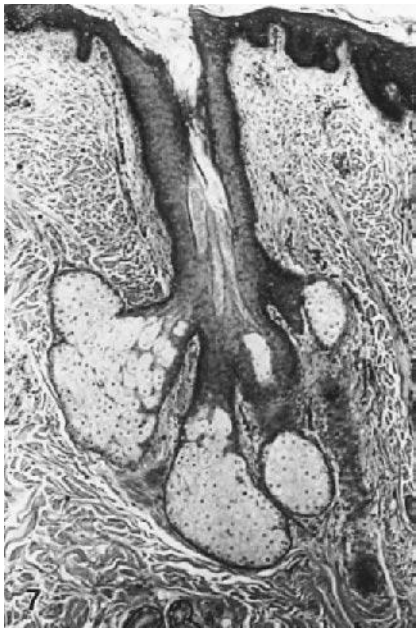

FIGURE 7 Sebaceous glands in skin of forehead. Hematoxylin and eosin. ×50.

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016

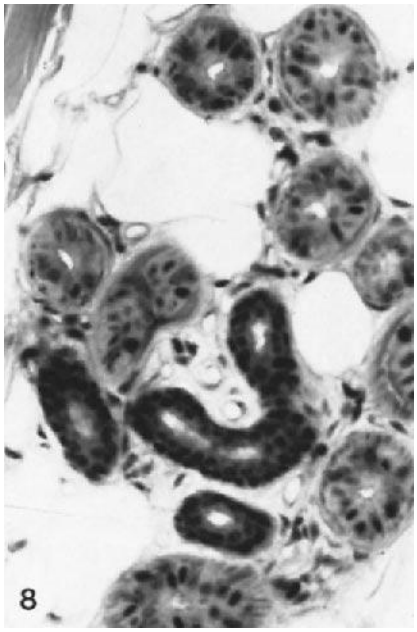

FIGURE 8 Section through a sweat gland. The pale structures are part of the secretory coiled tubule, the dark ones are part of the duct. Hematoxylin and eosin. ×250.

The coiled segment at the blind-ending terminus represents the secretory portion of the gland. This leads to the duct portion of the gland which is also coiled. The duct then ascends toward the surface. When it reaches the underside of the epidermis a spiralling channel through it conveys the secretion to the skin surface (Fig. 1). It is not understood how this channel remains patent in an epidermis whose keratinocytes are constantly proliferating and migrating.

When viewed with the light microscope the two parts of the gland can be easily distinguished from each other (Fig. 8). Compared to the duct, the secretory portion is wider, has a larger lumen, its epithelial lining cells appear pale and many myoepithelial cells are present. The latter are contractile cells that are part of the epithelium, lying within the basement membrane. Their contraction is thought to forcefully expel the secretion toward the skin surface. With the electron microscope, two types of epithelial lining cells are seen in the secretory portion. The so-called dark cells have an extensive contact with the lumen of the tubule and have secretory granules containing glycoprotein substances. The clear cells are distinguished by abundant glycogen in their cytoplasm. Continuous with the tubule lumen are many intercellular canaliculi between the clear cells. It is thought that the clear cells secrete a more or less isotonic solution via these channels into the lumen. The duct portion is lined by two layers of epithelial cells and lacks myoepithelial cells. It is thought that electrolytes are absorbed from the lumen here, making the sweat hypotonic by the time it reaches the surface of the skin.

ACKNOWLEDGMENTS

I would like to express my appreciation to Ms. Linda Prentice and Ms. Simona Ikeda for the photomicrographic work.

REFERENCES

1. S Banks-Schlegel, H Green. Involucrin synthesis and tissue assembly by keratinocytes in natural and cultured human epithelia. J Cell Biol 90:732–737, 1981.
2. PM Elias. Stratum corneum lipids in health and disease. In: Progress in Diseases of the Skin, Vol. 2, R. Fleischmajer, ed. Grune and Stratton, San Diego, 1984, pp. 1–19.
3. S Grayson, PM Elias. Isolation and lipid biochemical characterization of stratum corneum membrane complexes: implications for the cutaneous permeability barrier. J Invest Dermatol 78: 128–135, 1982.
4. RM Lavker, T Sun. Heterogeneity in epidermal basal keratinocytes: morphological and functional correlations. Science 215:1239–1241, 1982.
5. AM Lynley, BA Dale. The characterization of human epidermal filaggrin: a histidine-rich, keratin filament-aggregating protein. Biochim Biophys Acta 744:28–35, 1983.
6. T Murozuka, K Fukuyama, WL Epstein. Immunochemical comparison of histidine-rich protein in keratohyalin granules and cornified cells. Biochim Biophys Acta 579:334–345, 1979.
7. M Simon, H Green. Participation of membrane-associated proteins in the formation of the cross-linked envelope of the keratinocyte. Cell 36:827–834, 1984.
8. PW Wertz, DT Downing. Glycolipids in mammalian epidermis: structure and function in the water barrier. Science 217:1261–1262, 1982.
9. JG Zettergren, LL Peterson, KD Wuepper. Keratolinin: the soluble substrate of epidermal transglutaminase from human and bovine tissue. Proc Natl Acad Sci USA 81:238–242, 1984.

Marcel Dekker, Inc.
270 Madison Avenue, New York, New York 10016

Marcel Dekker, Inc.
270 Madison Avenue, New York, New York 10016

4

The Normal Nail

Josette André
Free University of Brussels and Hôpital Saint-Pierre, Brussels, Belgium

ANATOMY

The nail plate, also abbreviated to ''nail,'' is a hard keratin plate, slightly convex in the longitudinal and transverse axes. It is set in the soft tissues of the dorsal digital extremity, from which it is separated by the periungual grooves (proximal, lateral, and distal) (Fig. 1) [1,2]. It stems from the nail matrix located in the proximal part of the nail apparatus. The nail plate and matrix are partly covered by a skin fold called the proximal nail fold. The lunula, also known as ''half moon,'' is a whitish crescent visible at the proximal part of some nails and more specifically at those of the thumbs and big toes. It corresponds to the distal part of the matrix. From the latter, the nail plate grows towards the distal region, sliding along the nail bed to which it adheres closely and from which it only separates at the distal part, called hyponychium.

Two other structures deserve our attention:

1. The cuticle, which is the transparent horny layer of the proximal nail groove. It adheres to the nail surface and acts as a seal between the nail plate and the proximal nail fold.
2. The onychodermal band, which is ''orangey,'' is located in the distal region of the nail. It can be partly blanched by pressure, thus exsanguinating the region. It provides a zone of rugged attachment of the nail-to-nail bed.

The upper surface of the nail plate is smooth and has discrete longitudinal ridges that become more obvious with age (Fig. 2). The under surface is corrugated with parallel longitudinal grooves that interdigitate with the opposite ones of the nail-bed surface, enhancing the adhesion of the nail plate to the nail bed.

HISTOLOGY

The nail plate is made up of parallel layers of keratinised, flat, and completely differentiated cells with no nucleus. Three zones can be identified at the distal part of the nail: the upper (or dorsal) nail plate which makes up one third of the nail; the lower (or ventral) nail plate which makes up two thirds of the nail; and the subungual keratin. The latter corresponds to the thick, dense, horny layer of the hyponychium (Fig. 3) [3,4].

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016

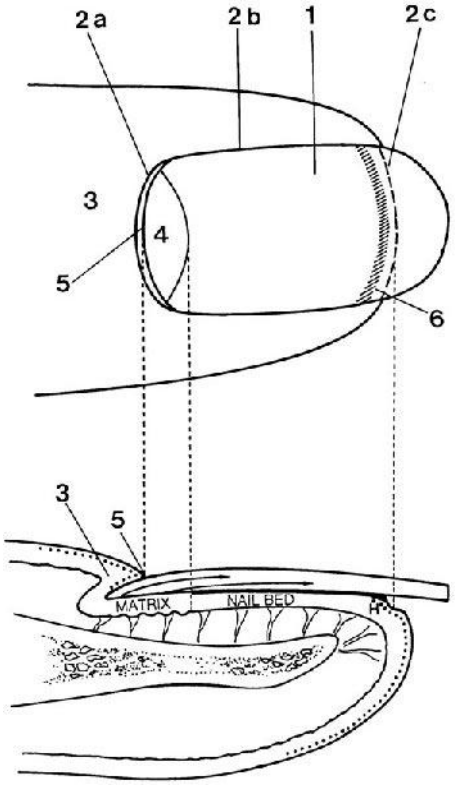

FIGURE 1 The normal nail. (1) nail plate, (2) nail grooves [(2a) proximal nail groove, (2b) lateral nail groove, (2c) distal nail groove], (3) proximal nail fold, (4) lunula, (5) cuticle, (6) onychodermal band, H, hyponychium, small dots, stratum granulosum.

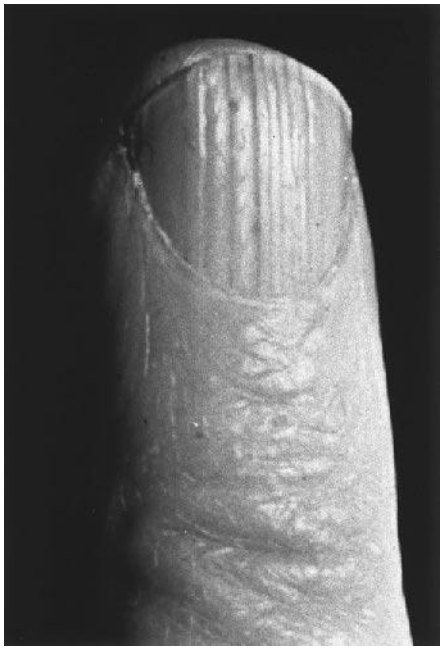

FIGURE 2 Obvious longitudinal ridges on the nail surface, as noticed in older people.

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016

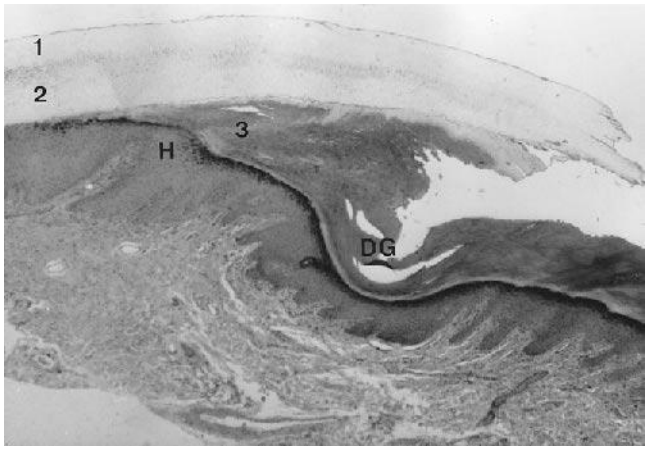

FIGURE 3 Longitudinal section of the distal part of the nail apparatus. (1) upper or dorsal nail plate, (2) lower or ventral nail plate, (3) subungual keratin. H, hyponychium; DG, distal groove.

In electron microscopy (Fig. 4) [5], the nail plate cells appear to be made of a regular weft of keratin filaments within an interfilamentous matrix. In the upper (or dorsal) nail plate, cells are flat, their cellular membranes are discreetly indented, and they are separated from each other by ampullar dilatations. At the surface, those cells are piled up like roof tiles, which gives the nail surface its smooth aspect. In the lower (or ventral) nail plate, cells are thicker, their cellular membranes are anfractuous, and they interpenetrate through extensions, making real anchoring knots that seem to be partly responsible for nail elasticity.

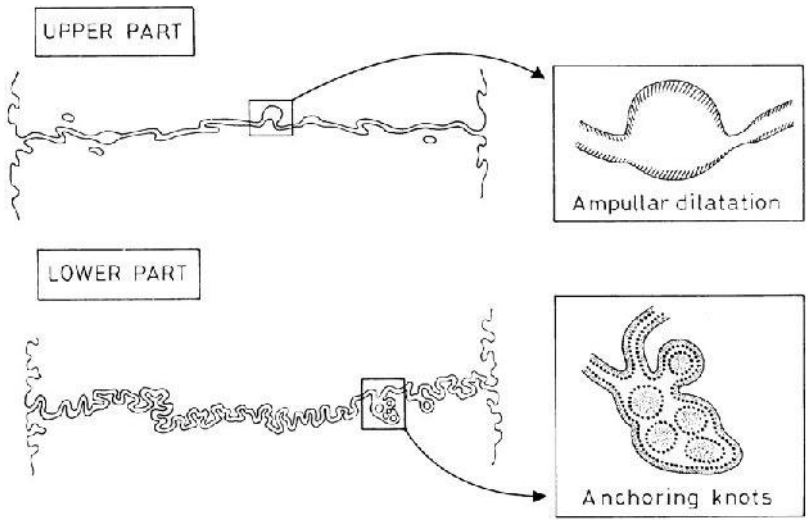

FIGURE 4 Schematic drawing of the cell membranes in the dorsal and ventral part of the nail plate, as observed in electron microscopic examination. (From Ref. 5.)

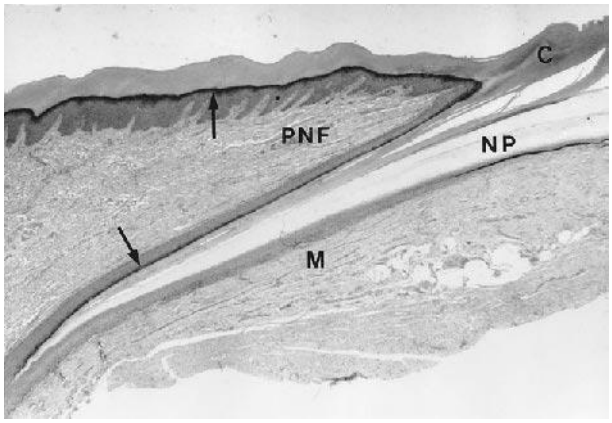

FIGURE 5 Longitudinal section of the proximal part of the nail apparatus. PNF, proximal nail fold; C, cuticle; NP, nail plate; M, matrix. A stratum granulosum (arrows) is present in the dorsal and ventral part of the proximal nail fold epithelium but absent in the matrix epithelium.

A longitudinal section of the nail apparatus enables us to visualize most characteristics of the other ungual structures (Fig. 1). From the proximal to the distal region, the following are identified:

- The proximal nail fold (Fig. 5). Its dorsal part is in continuity with the epidermis of the digit back. Its ventral part is a flat and rather thin epithelium that keratinizes with a stratum granulosum. The cuticle corresponds to the stratum corneum of the most distal part of the proximal nail fold, at the angle of the dorsal and ventral part.
- The nail matrix is a multilayered epithelium characterized by an abrupt keratinization without interposition of keratohyaline granules (Fig. 5). It gives birth to the nail plate: the proximal part of the matrix gives birth to its dorsal part and the distal part of the matrix gives birth to its ventral part. The epithelium of the matrix also contains melanocytes and Langerhans cells. Most melanocytes are dormant [6] and do not produce pigment. However, in dark-skinned individuals, longitudinal pigmented bands can be observed in nails. This racial physiological pigmentation is attributable to the activation of the matrix melanocytes and to the melanin incorporation in the nail plate (longitudinal melanonychia). It usually affects several nails and tends to become more frequent with aging; this can only be observed in 2.5% of 0- to 3-year-old black children but in 96% of blacks older than 50 years of age (Fig. 6) [7].
- The nail bed epithelium, like the one of the matrix, keratinizes abruptly. The stratum granulosum reappears only at the hyponychium, which represents the distal thickened part of the nail bed and is bordered by the distal groove and the digital pulp (Fig. 3). Melanocytes are rare in the nail bed.

The nail apparatus is strongly attached to the periosteum of the distal phalanx by thick collagen bundles. Elastic fibers are rare and eccrine sweat glands are absent.

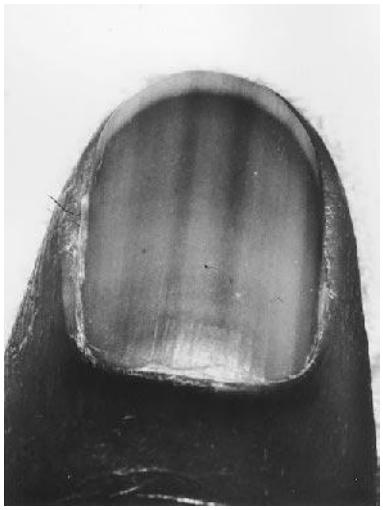

FIGURE 6 Multiple longitudinal melanonychia in an adult black patient.

PHYSICOCHEMISTRY

The nail is highly rich in keratins, specially in hard keratins which are close to those of hair and have a high content of disulfide linkage (cystine) [1,2]. The high sulfur-containing keratins play an important role in the nail toughness and presumably in its good barrier property as well.

Sulfur represents 10% of the nail's dry weight; calcium represents 0.1 to 0.2%. The latter, contrary to conventional wisdom, does not intervene in the nail toughness.

Lipid content (particularly cholesterol) is low in nails: from 0.1 to 1% compared with 10% in the stratum corneum of the skin. Water concentration varies from 7 to 12% (15–25% in the stratum corneum) but the nail is highly permeable to water: when its hydration level increases, it becomes flack and opaque and when its hydration level drops, it becomes dry and brittle.

Studies carried on nail permeability are important for the development of cosmetic and pharmaceutical products specifically devoted to nails [8]. As a permeation barrier, it has been shown that the nail plate reacts like a hydrogel membrane, unlike the epidermis which reacts like a lipophilic membrane.

The normal nail is hard, flexible, and elastic, which gives it good resistance to the microtraumatisms it undergoes daily. Those properties are attributable to the following factors: the regular arrangement and important adhesion of keratinocytes, the anchoring knots, the high-sulfur–containing keratins and the hydration level of the nail.

PHYSIOLOGY

The nail grows continuously. In 1 month, fingernails grow about 3 mm and toenails grow about 1 mm. A complete renewal therefore takes 4 to 6 months for normal fingernails whereas 12 to 18 months are needed for toenails [1,2].

The origin of nail plate production is still a debatable point. At least 80% of the nail plate is produced by the matrix, and the main source of nail plate production is the

proximal part of the matrix. This probably explains why distal matrix surgery or nail bed surgery has a low potential for scarring compared with proximal matrix surgery [9]. Some studies suggest that the nailbed produces 20% of the nail plate, whereas others suggest that the nail bed hardly participates in the making of the nail plate [9,10].

The nail plays an important role in everyday life. It protects the distal phalanx from traumatisms it undergoes regularly. It plays a role in the sensitivity of the digital extremity and intervenes more specifically in the picking up of small objects such as needles. The nail allows scratching in case of itching and can be used as a means of attack or defense. Finally, the aesthetic importance of the nail should not be neglected.

AESTHETICS

For centuries the nail has played an important aesthetic role. Having clean nails is essential to looking well groomed and refined, and among women nails also need to be long and painted.

A ''good-looking'' nail has a smooth and shiny surface. It is transparent and adheres to its bed. Regarding the proximal groove, the cuticle has to be intact and thin. The distal and the lateral grooves have to be clean and the periungual tissues must be without hangnails and sores. The free border has to be smooth; its shape can be round, pointed, oval, or square. Women often wear long fingernails cut oval, which makes fingers look longer and thinner. Yet, square nails are in fashion. Too-long nails can look unpleasant and can even be a nuisance.

Men wear short fingernails cut square. Both women and men have short toenails cut square. A normal nail structure and appropriate cosmetic care are necessary to obtain such ''good-looking'' nails.

REFERENCES

1. RPR Dawber, D de Berker, R Baran. Science of the nail apparatus. In: R Baran, RPR Dawber, eds. Diseases of the Nails and Their Management. 2d ed. Oxford: Blackwell Scientific Publications, 1994, pp. 1–34.
2. D de Berker. The normal nail. In: J André, ed. CD-ROM: Illustrated Nail Pathology. Diagnosis and Management. Antwerpen: Lasion Europe, 1995.
3. G Achten, J André, M Laporte. Nails in light and electron microscopy. Semin Dermatol 10: 54–64, 1991.
4. J André, M Laporte. Ungual histology in practice. In: J André, ed. CD-ROM: Illustrated Nail Pathology. Diagnosis and Management. Antwerpen: Lasion Europe, 1995.
5. D Parent, G Achten, F Stouffs-Vanhoof. Ultrastructure of the normal human nail. Am J Dermatopathol 7: 529–535, 1985.
6. Ch Perrin, JF Michiels, A Pisani, JP Ortonne. Anatomic distribution of melanocytes in normal nail unit. An immunohistochemical investigation. Am J Dermatopathol 19:462–467, 1997.
7. JJ Leyden, DA Spott, H Goldschmidt. Diffuse and banded melanin pigmentation in nails. Arch Dermatol 105:548–550, 1972.
8. Y Sun, J-C Liu, JCT Wang, P De Doncker. Nail penetration. Focus on topical delivery of antifungal drugs for onychomycosis treatment. In: RL Bronaugh, HI Maibach, eds. Percutaneous Absorption. Drugs-Cosmetics-Mechanisms-Methodology, 3rd ed. New York: Marcel Dekker, 1999, pp. 759–778.
9. D de Berker, B Mawhinney, L Sviland. Quantification of regional matrix nail production. Br J Dermatol 134:1083–1086, 1996.
10. M Johnson, S Shuster. Continuous formation of nail along the bed. Br J Dermatol 128:277–280, 1993.

Marcel Dekker, Inc.
270 Madison Avenue, New York, New York 10016

5

Hair

Ghassan Shaker and Dominique Van Neste
Skinterface sprl, Tournai, Belgium

INTRODUCTION

Hair is a symbol of good looks and beauty in some areas of the human body. So much time, effort, and money are spent in caring for it, especially in the case of scalp hair. In some other areas, like the beard, daily care by shaving is necessary for the majority of males. In females, abundant scalp hair is very much welcomed, unlike leg hair, facial hair, and armpit (axillary) hair. Hair distribution in certain body regions is a secondary sex characteristic and starts to appear around puberty as the beard, moustache, and body hair in males, and pubic and axillary hair in both sexes.

The social meaning of hair is very important. So many old and present social and/or religious practices deal with hair. Enforced shaving of scalp hair has long been used as a sign of punishment and in certain religious practices as a sign of obedience. The Romans completely shaved the scalps of prisoners, adulterers, and traitors. Scalping the warring enemies, which was long practiced by some primitive societies was meant to express victory and revenge [1].

Hair styling can serve as a form of expression. Rebellion of youth to the existing social order is often manifested as a change in appearance, and especially change of hair style, e.g., long hair on males, shaved hair (skinheads), and dyed hair (punks) [1].

Hair also plays a role as a distinguishing sign of one's ethnicity, varying from straight to curly in form and from dark to blond in color. There is also a difference in the amount of body hair between races. Hair is generally subject to so much interracial and interindividual variation that it can be said that, apart from the hair follicle, there is no organ in the human body that is morphologically so much variable as hair.

Although hair is not vital to human existence, it is greatly important to one's psychological equilibrium [2–4]. Psychological problems of hair loss occur in both sexes, and more among women because of the relevance of physical attractiveness [5]. Hair is closely related to physical attractiveness and the difference between male and female hair patterning provides a recognition phenomenon. In general, baldness leads to overestimation of age of affected males [1].

In addition to the aesthetic function of hair, it has more natural functions, which are becoming less important because of the anthropological evolution and technical prog-

Marcel Dekker, Inc.
270 Madison Avenue, New York, New York 10016

ress of mankind. Scalp hair protects against certain environmental conditions like sun rays and cold. Body hair in man is very much reduced in comparison with other mammals, and many theories have been postulated to explain this fact; most are based on temperature and thermal regulation of the human body all along the course of the evolution of mankind. Nasal hair protects against dust and acts as an air filter. Axillary and perineal hair reduce the friction during body movement and also serve for the wider or prolonged dissemination of apocrine gland odor. Pubic hair is said to have some excitatory functions during sexual intercourse.

Innumerable are the cosmetic products intended for use in hair care to remove sebum and dirt and to improve the look, shininess, uniformity, softness, color, odor, and ease of comb of the hair, as well as deposition of conditioning molecules and reduction of static ''fly-aways'' (e.g., shampoos, conditioners, hair dyes, fixation sprays, gels, creams, etc.) There are also many products that have been marketed and used by people as anti–hair loss preparations and/or hair growth–promoting agents. Many have not stood the test of time. Ancient medical literature is full of pharmaceutical prescriptions and formulas to be used to treat hair loss or to promote hair growth. They are so diverse in source and nature that any attempt to categorize them seems useless.

In addition to scalp hair formulas, many other compounds are intended to remove or to assist the removal of hair from other parts of the body, e.g., preshave and aftershave preparations, depilatories, and so on. Other products aim to decrease the contrast of hair with the skin, making hair less visible, e.g., bleaching agents. Besides the variable efficacy of these products, consumers may develop many nonintended effects on the hair and skin such as hair damage, hair loss, skin irritation, and/or allergy and photoreactions attributable to some active ingredients and/or their additives. In order to understand hair production, it is necessary to revisit the embryogenesis and to have an idea about the structure and functional activity of the hair follicle. These aspects will now be briefly described.

THE HAIR FOLLICLE

Embryology

In the early stages of hair follicle development in human fetal skin, a simultaneous differentiation of some epidermal and dermal cells takes place between the second and third months of intrauterine life in some areas such as the eyebrows and chin, followed by other body regions in the fourth month. Histologically, it begins as a crowding of cells in the basal layer of the epidermis with a simultaneous aggregation of mesenchymal cells directly beneath the developing epithelial component. Cells in the basal layer elongate to form the hair peg, which grows obliquely downwards in an orientation characteristic for each body region. The broad tip of the hair peg will become slightly concave and carries before it the aggregated mesenchymal cells, which will become the dermal papilla. During the downward course of the hair peg, two swellings appear at the posterior side of the follicle. The upper swelling will form the sebaceous gland, whereas the lower will become the insertion site of the arrector pili muscle. In some body sites, such as the axilla, groin, skin of genitalia, and face, a third swelling is going to develop above the sebaceous gland bud and this will form the apocrine gland [6–8].

Hair follicle development proceeds in a cephalocaudal direction and is completed

by the 22nd week of intrauterine life. These follicles progressively synthesize hair shafts (lanugo hair), which are visible at the cutaneous surface by the 28th week. The first hair coat of fine lanugo hair is shed in utero at about 1 month before birth at full term. The shedding course follows a cephalo caudal direction, which means that frontal hair follicles begin their second hair cycle while occipital hair follicles are still in their first hair cycle. The second coat of lanugo hair is going to shed from all areas during the first 3 to 4 months of life [6–8].

Histology

The hair follicle bulb is composed of a central dermal papilla and a surrounding hair matrix. It undergoes many changes according to the cyclical activity of the hair follicle in health and disease. At the level of attachment of the arrector pili muscle to the follicle is the bulge zone of the root sheaths. This is considered to be the stem cell site from which a new hair cycle is initiated. The hair shaft is enclosed in two sheaths, i.e., the inner root sheath and the outer root sheath. The inner root sheath consists of a cuticle layer on the inside (next to the cuticle layer of the hair cortex), Huxley's layer in the middle, and Henle's layer on the outside. The inner root sheath hardens before the presumptive hair within it, and it is consequently thought to control the definitive shape of the hair shaft [6–8].

The outer root sheath cells have a characteristic vacuolated aspect. This sheath is covered by the vitreous membrane. Next to this layer we can find the connective tissue sheath with its characteristic fibroblasts [6–8].

Cyclical Activity

Production of a hair segment by a hair follicle undergoes a cyclical rhythm. Activity (anagen) is followed by a relatively short transitional phase (catagen) and a resting phase (telogen) (Fig. 1). The duration of activity or anagen varies greatly with species, body region, season, age, and the type of hair (i.e., terminal or vellus).

In adult humans the activity of each follicle is independent of its neighbors (asynchronous). However, during the development of the human embryo as well as the early months of life, there is a more or less synchronous moult of scalp hairs. Each follicle goes through the hair cycle a variable number of times in the course of a lifetime. On average, at any one time about 13% of the scalp hair follicles are in telogen and only 1% or less are in catagen. Telogen ratio may count higher in certain stressful physical and/or mental conditions such as telogen effluvium and postpartum alopecia [6–8].

HAIR STRUCTURE

Postnatal hair may be divided into two broad categories: vellus hair, which is soft, unmedullated, occasionally pigmented, and seldom exceeds 2 cm in length; and terminal, which is longer, coarser, and often pigmented and medullated [8]. Before puberty, terminal hair is limited to the scalp, eyebrows, and eyelashes. After puberty, secondary sexual terminal hair is developed from vellus hair in response to androgens. The bulk of any hair segment is formed mainly by the cortex, which is surrounded by a cuticle and may also have a continuous or discontinuous core or medulla [8,9]. The medulla is usually found in thicker

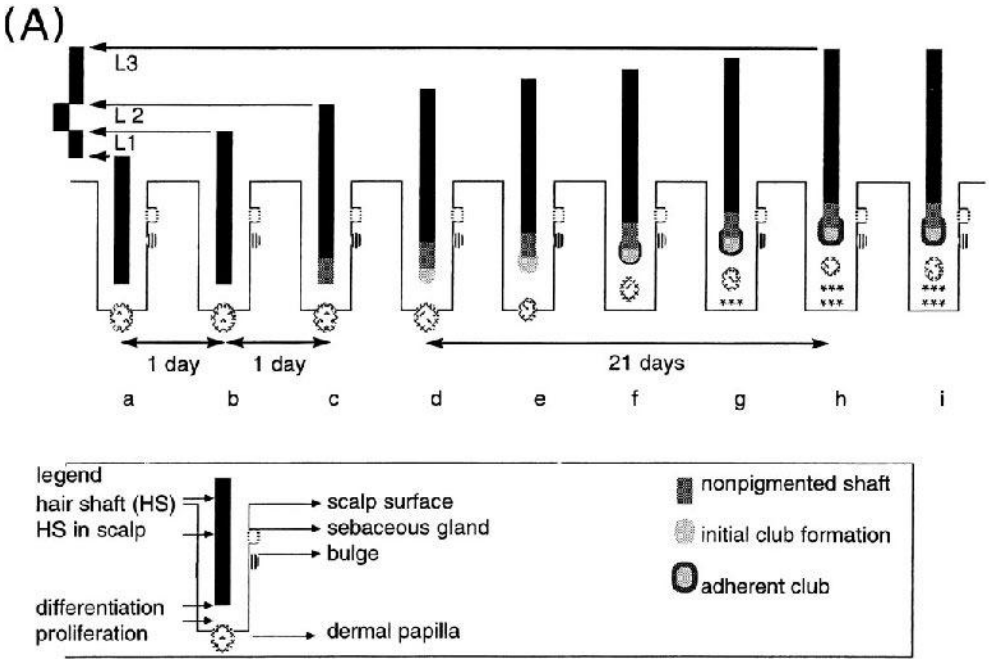

FIGURE 1 Schematic view of hair cycling of a human hair follicle. The latest steps of the hair-growth phase (anagen 6) during which hair is visible at the skin surface and growing are shown in (A) while the apparent rest phase of the hair cycle (telogen phase) is shown in (B) during which a new hair cycle can be initiated. The legend [between (A) and (B)] helps the reader to orient himself within the various components of the human hair follicle, which are essential to understanding growth and rest.

(A) *From growth to rest*: The same hair follicle is represented at various times (days) at the very end of the growth phase. At the skin surface, there is normal pigmented hair production (days a–b and b–c) representing the constant daily hair production (L1 and L2). Then, the pigmentation of the newly synthesized hair shaft (appearing at the bottom of the hair follicle) is decreased (c). This early event announces the regression of the impermanent portion of the hair follicle and is followed by terminal differentiation of cells in the proliferation compartment (d) and shrinkage of the dermal papilla (e). The latter starts an ascending movement together with the hair shaft (f–h; 21 days). This characterizes the catagen phase (d–h). The apparent elongation of the hair fiber (L3) reflects the outward migration of the hair shaft. What is left after disappearance of the epithelial cells from the impermanent portion of the hair follicle is, first, basement membranes, followed by dermal connective tissue usually referred to as streamers or stelae (***). The true resting stage begins when catagen is completed, i.e., when the dermal papilla abuts to the bottom of the permanent portion of the hair follicle. In the absence of physical interaction between dermal papilla and bulge the next cycle (see B) is definitely compromised. As from now no hair growth is observed at the surface (h–i).

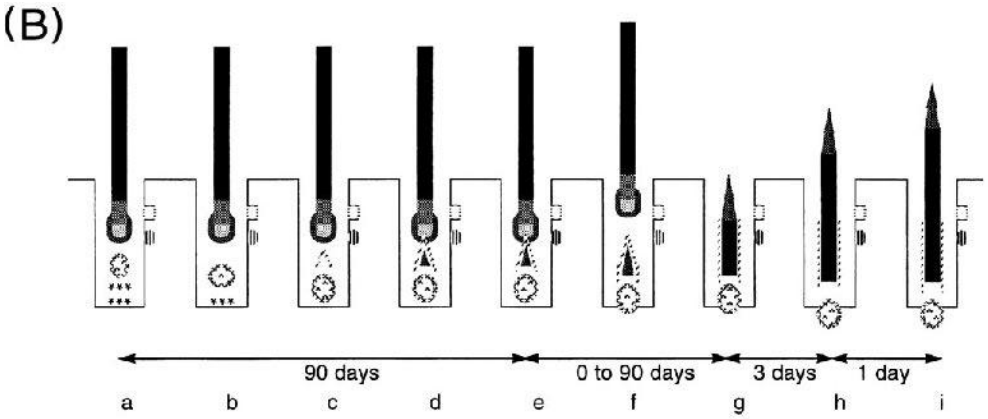

FIGURE 1 Continued (B) *From rest to growth*: During this stage, one notices absence of hair growth at the skin surface (a–g) but significant changes occur in the deeper parts of the hair follicle. The dermal papilla expands and attracts epithelial cells from the bulge (stem cell zone) in a downward movement (a–b). To create space, previously deposited materials have to be digested (a–b, *). The epithelial cells then start differentiation in an orderly fashion starting with the inner root sheath (c) and the tip of the cuticle and hair cortex of the newly formed unpigmented hair fiber (d). The resting hair remains in the hair follicle for approximately 1 to 3 months (a–e), then the detached hair is shed (f). The shiny root end of the shed hair is the club. Before, during, or after hair shedding there may be replacement by a new hair shaft (e–f–g). Indeed, under physiological conditions, the follicle proceeds immediately or only slowly with new hair production (from f to g; maximum 90 days). Certain conditions are characterized by a much longer interval before regrowth is visible. Usually, a nonpigmented hair tip is seen first (h), followed by a thicker, more pigmented, and faster-growing hair fiber (i) depending on the many regulatory factors controlling the hair follicle. (Reproduced with permission from H.A.I.R. Technology [Skinterface sprl, Tournai, Belgium].)**

hair, and its protein composition contains trichohyaline. Above the level of the epidermis some medullar cells dehydrate, forming air-filled vacuoles, which are responsible for the interrupted appearance of the medulla because of the reflection of light on these air-filled spaces. The mature cortex consists of closely packed spindle-shaped cells separated by intercellular lamella cementing the cells together. Within the cells most of the microfibrils are closely packed and oriented longitudinally [8,9].

The hair cuticle consists of five to 10 overlapping cell layers imbricated like roof tiles and aimed outwards (towards the distal end of the hair). The mature cells are thin scales consisting of dense keratin. Over the newly formed part of the hair the scale margins are intact, but as the hair emerges from the skin they break off progressively. The outer surface of each cuticular cell has a very clear A-layer, which is rich in high-sulfur protein; this layer protects the cuticular cells from premature breakdown caused by chemical and physical insults [8,9].

Keratins are a group of insoluble cystine-containing helicoidal protein complexes produced in the epithelial tissues of vertebrates. Because of the resistance of these protein complexes, hairs have been said to contain hard keratins as opposed to the soft keratins of desquamating tissues [9].

CLINICAL HAIR-GROWTH–EVALUATION METHODS

Subjective evaluation and personal satisfaction of people using hair-growth modulators and/or cosmetics on a wide scale are the most important factors for the survival of these products in the market. This evaluation will be based on whether they are perceived as efficacious, especially when the benefit is cosmetic in nature (acknowledging the massive placebo effect and the possible bias). Hence, before they reach the hands of consumers, safety and efficacy testing have to be performed according to the science, ethics, and rules of good clinical practice and medical research in order to adequately support the claims made to the patient and the consumer.

For an evaluation method to be considered valuable, it should provide information about the following variables: hair density, which is the number of hairs per unit area (usually number/cm^2); linear hair growth rate (LHGR) as millimeters per day; percentage of anagen growth phase (%A); hair diameter in micrometers; and time to hair regrowth after completion of telogen phase [10]. For many evaluation techniques, the methodology details are lacking as well as information about sensitivity and reproducibility usually required for clinical investigative techniques [11]. Much effort is needed for the standardization of evaluation methods in order to make it possible to compare different methods, or different results from different centers using the same method. For classification purposes these methods can be categorized as invasive, semi-invasive, and noninvasive.

Invasive methods

Biopsy

In addition to the ordinary vertical sectioning of skin biopsies which permits the study of longitudinal follicular sections, horizontal sectioning (parallel to the skin surface) of scalp biopsies offers further diagnostic opportunities. First described by Headington [12], it has been demonstrated that horizontal sectioning may provide a better diagnostic yield than vertical sectioning [13,14]. Horizontal sectioning allows the study of larger number of follicular structures. Inflammatory infiltrates are more easily seen and their relationship to the follicular structures is more obvious than in vertical sectioning. Fibrous tracts, which are often difficult to visualise on vertical sectioning, become much more apparent on horizontal sectioning. It is possible as well to distinguish vellus from terminal hairs, to identify the stages of all hairs in one section and to classify them into anagen, telogen or catagen follicles.

Semi-invasive Methods

Trichogram

The idea of estimating changes affecting hair growth by examining hair roots was first suggested by Van Scott et al. [15]. In order to examine hair root status necessary to diagnose hair disorders, at least 50 hairs should be plucked in order to reduce sampling errors. The roots are examined under a low-power microscope. The root morphology is stable and hairs can be kept for many weeks in dry packaging before analysis. Due to the relative values generated telogen/anagen (T/A) ratio, this technique is a relatively poor indicator of disease activity and/or disease severity in androgen-dependent alopecia in women [16]. In our center this method has been abandoned because it generates only relative values as compared with the method described in the following section.

Marcel Dekker, Inc.
270 Madison Avenue, New York, New York 10016

Unit Area Trichogram

The unit area trichogram (UAT) is a technique in which all the hairs within a defined area (usually 60 mm^2) are plucked and mounted onto double-sided tape attached to a glass slide. Optical microscopical examination of these slides estimate various hair variables as hair density, anagen%, hair length and hair diameter. The scalp area to be sampled should first be degreased (with an acetone/isopropanol mixture) and then delineated with a roller pen. All hairs contained in the area are epilated individually (one by one). Each hair is grasped at a uniform point above the scalp and the forceps are rotated to ensure firm grasp. Epilation should be performed rapidly in a single action in the direction of hair growth orientation, in order to minimize trauma to the roots [17].

The unit area trichogram is one of the rare exceptions to a strange general rule or law in trichology; indeed, most methods are promoted along with a new drug or a new cosmetic efficacy evaluation program. The exception in the unit area trichogram is that the method has been evaluated independently in terms of reproducibility and clinical relevance. Therefore, it could serve for comparative purposes. Most hair-growth variables estimated through unit area trichogram and the phototrichogram are comparable. However, the unit area trichogram has the advantage in that it can be used reliably in subjects in whom there is no contrast between hair and skin color [18].

Noninvasive Methods

Global Methods

Scoring Classification Systems The patterns produced by the gradual process of scalp hair loss in male pattern baldness were first described by Hamilton in 1951. In 1975, Norwood proposed a modification of Hamilton's classification. In this modification he mentioned three patterns that referred to women. Finally, in 1977 Ludwig published the stages of female androgenetic alopecia in three patterns. For more details we refer the interested reader to the following references: Camacho F, Montagna W [19] and Ludwig E, Montagna W, Camacho F [20]. Although static by definition, such diagrams can be enriched by more gradual variations [8], an updated version of which appears in Figure 2, but these will only rarely match the continuum that one observes in the hair clinic.

Global Photography Global photography apprehends all factors involved in hairiness at once and can be used for drug efficacy evaluation provided that adequate scalp preparation and hair style are maintained throughout the study. This is the most patient-friendly photographic method. This method is used in the clinic under standardized conditions of exposure [21]. Processing and rating have to be performed under controlled (i.e., blinded as to treatment and/or time) conditions. Trained raters could generate reproducible data.

Daily Collection of Shed Hair The cyclic hair growth activity results in a daily shedding process in which telogen hairs are shed to be replaced by anagen hairs. The reported normal average daily loss of hair ranges somewhere between 40 to 180 hairs per day. In a study of 404 females without hair or scalp disease, lost hair was collected daily over 6 weeks in the aim of comparing two shampoos. Results showed mean hair loss rates ranging from 28 to 35 per day. No significant differences were noted in the mean daily hair loss rates during the 2-week baseline and the 4-week treatment period [22].

Marcel Dekker, Inc.
270 Madison Avenue, New York, New York 10016

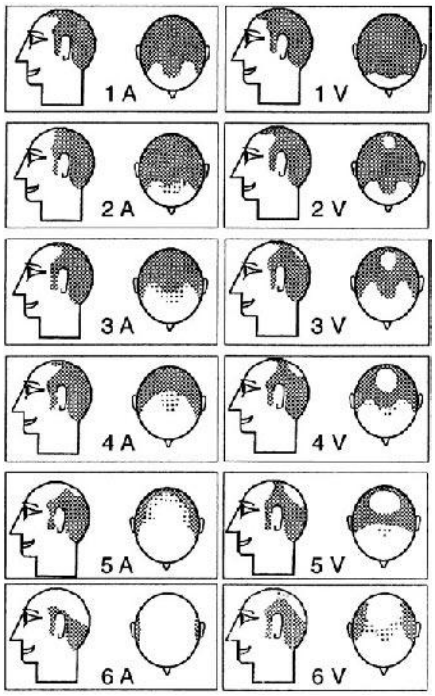

FIGURE 2 Scoring of androgen-dependent alopecia (ADA) in men. The present classification shows ADA patterns that affect the scalp of genetically susceptible male subjects after puberty. They are subdivided in six stages from mild to severe balding (1–6). The anterior pattern (A) indicates a backward progression of hair follicle miniaturization and deficient hair production with the ensuing bald appearance. The vertex type (V) indicates isolated regression occurring on the vertex but this is usually combined with the involvement of the frontal temporal areas. (Reproduced with permission from H.A.I.R. Technology [Skinterface sprl, Tournai, Belgium].)

Quantitating daily hair loss in women was assessed in another study of 234 women complaining of hair loss among which 89 had apparently normal hair density. They have found that subjects with normally dense hair (although complaining about hair loss) shed less than 50 hairs a day [16]. So the magic number of 100 so often referred to in textbooks and found in the lay press should be seriously revisited. Less than 50 hairs can be significantly abnormal in a patient having lost 50% of his hair. Further standardization studies are currently being run in our laboratory.

Hair Weight and Hair Count The efficacy of hair-growth–promoting agents can be established by comparing the total hair mass (weight) and counts of grown hair in a small, carefully maintained area of the scalp [23,24]. A plastic sheet with a 1.2 cm^2 hole was placed over the selected site. All hairs within the square hole were pulled through it and hand clipped to 1 mm in length. The apparent advantage of this method is that it provides a global measurement of growth on a small sample size for the detection of drug effects and between treatment regimens (e.g., 2 vs. 5% minoxidil) [24]. One must be aware of the technical skills necessary to handle the samples in the proper way to avoid the loss of some hairs between the clinic and the laboratory. Again, as for many of these

techniques, the methodological comparisons are lacking and there are no evaluations of the reproducibility and sensitivity usually required for laboratory evaluation methods because they were introduced on the occasion of drug evaluation protocols. The major limitation of this method is that it generates a global index of growth, the individual components of which cannot be analyzed separately.

Hair-Pull Test The hair-pull test is based on the idea that ''gentle'' pulling of the hair brings about the shedding of telogen hairs [16]. It is a very rough method and difficult to standardize because it is subject to so much interindividual variation among the investigators. Physically speaking, the pulling force is not uniformly distributed over the whole hair bundle, thereby creating variation in the pulling force from one hair to another. It seems to be useful only in acute and severe conditions, not in chronically evolving conditions like androgen-dependent alopecia.

Analytical Methods

Phototrichogram The basic principle of the phototrichogram (PTG) consists of taking a photograph of a certain area of the scalp in which the hair is cut in preparation for the photograph, and to repeat this photographic documentation after a certain time period. This period of time should be long enough to permit the evaluation of the growth of a hair segment (which is usually between 24-72 h). The growth is then evaluated by comparing the two pictures. Hairs that have grown are in anagen phase and those that have not are in telogen phase (Fig. 3).

The assessment is made on defined scalp sites considered representative of the condition. The data that can be generated from a PTG include the total number of hairs present in a certain surface area, which allows us to calculate hair density (N/cm^2). Hair density is a quantitative element through which we can estimate the degree of hair loss.

Also from a PTG, we can determine the percentage of hairs in the growth phase

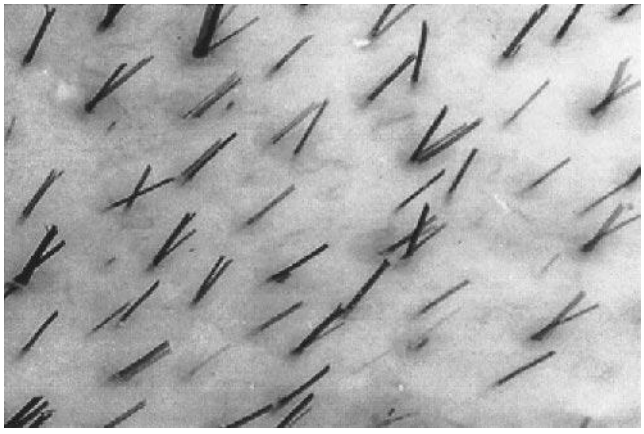

FIGURE 3 Day 2 picture of scalp hair (48 hrs after clipping short all scalp hairs from the photographed scalp site): long growing hairs represent follicles in anagen phase; shorter nongrowing hairs represent follicles in telogen.

(anagen%) and can calculate the LHGR. Meanwhile, the reliability of the evaluation of hair thickness has been the subject of detailed analysis. The most precise instrument used for hair-diameter evaluation remains the microscope.

One of the main advantages of the PTG is that first of all it is a patient-friendly method. Secondly it is a totally noninvasive method so it does not affect the natural process of hair growth/loss by itself. However, many patients are afraid of the idea of having their hair cut at one or more given scalp surface sites (area $\pm$ 1 cm^2 in our protocol). Most are reassured by the fact that this process cannot prevent them from enjoying a normal private and social life. Finally, PTG also permits the chronological follow-up of exactly the same area under the study, and this has been shown to bring about a lot of valuable information [25]. Some technical improvements have been introduced during the course of evolution of the PTG technique. For example, the application of a frontal window with a glass slide mounted on it has been considered a major improvement [26,27]. It reduces the curvature of the scalp and permits a better image clarity.

Some technical photography problems have been identified during the course of the evolution of the PTG, and a series of detailed analysis performed at our laboratory and clinic have pinpointed a number of them, including the primary enlargement factor (PEF), which is one of the factors responsible for the ''visibility'' of hair on a photograph [28]; the secondary enlargement factor (size of printouts); and the experience of technicians. A further improvement was the development of scalp immersion proxigraphy (SIP), which is routinely used at our hair clinic and permits a better diffusion of light through a medium of lower optic heterogeneity [29].

After comparison with UAT [18], weak points of the method have been considered with great care, and using photography in combination with hair-micrometry results in a valid method for global hair perception while allowing an analytical description of all variables intervening in hair-quality evaluation.

Variants of Phototrichogram

Video PTG In this method, the photographic camera is replaced by a video camera equipped with specific lenses. In fact, recent reports in which this method has been used have been on Asians. In these subjects the contrast between hair and scalp seems favorable for the application of this method. Moreover, the reported low figures of hair density could possibly be racial in origin. However, we advise taking these factors into account in order to keep the biological variation as low as possible [30]. The recent introduction of cheap CCD cameras will certainly contribute to further developments in this field.

Traction PTG This test is based on the fact that hairs that can be easily pulled from the scalp are in telogen and those resisting pull are in anagen [31]. This test has been performed on a surface area of 0.25 cm^2. Hairs present at this surface area are held gently between the thumb and index fingers and pulled repeatedly. Hairs that can be easily pulled are counted and their number is considered the number of telogen hairs. Those resisting pulling are clipped and counted, and their number represents the anagen hairs. Through this method, we can calculate the hair density per unit area as well as the anagen%.

It is necessary to evaluate this semi-invasive method more critically to define its reproducibility through the standardization of the pulling technique. Other comparative studies may be essential as well to estimate the sensitivity and specificity of this method,

Marcel Dekker, Inc.
270 Madison Avenue, New York, New York 10016

which as it stands today would be rated as flawed with many weak points (e.g., small surface area, lack of control on traction forces etc.).

REFERENCES

1. Van der Donk A. Psychological aspects of androgenetic alopecia. Thesis, University of Rotterdam, The Netherlands, 1992.
2. Passchier J. Quality of life issues in male pattern hair loss. Dermatology 1998; 197:217–218.
3. Girman CJ, Rhodes T, Lilly FRW, Guo SS, Siervogel RM, Patrick DL, Chumlea WC. Effects of self-perceived hair loss in a community sample of men. Dermatology 1998; 197:223–229.
4. Cash TF. The psychological effects of androgenetic alopecia in men. J Am Acad Dermatol 1992; 26:926–931.
5. Cash TF, Price VH, Savin RC. Psychological effects of androgenetic alopecia on women: comparison with balding men and with female control subjects. J Am Acad Dermatol 1993; 29:568–575.
6. Montagna W, Camacho F. The anatomy and development of hair, hair follicles, and the hair growth cycles. In: Camacho F, Montagna W, eds. Trichology: Diseases of the Pilosebaceous Follicle. Madrid: Aula Medica Group, 1997:1–27.
7. Messenger AG, Dawber RPR. The physiology and embryology of hair growth. In: Dawber R, ed. Diseases of the Hair and Scalp. 3rd ed. Oxford: Blackwell Science Ltd, 1997:1–22.
8. Dawber R, Van Neste D. Hair and Scalp Disorders. London: Martin Dunitz Ltd, 1995.
9. Zviak C. The Science of Hair Care. New York: Marcel Dekker, 1986.
10. Van Neste D. Hair growth evaluation in clinical dermatology. Dermatology 1993; 187:233–234.
11. Trancik RJ. Physical methods for human hair evaluation. In: Van Neste D, Randall VA, eds. Hair Research for the Next Millenium. Amsterdam: Elsevier, 1996: 84–85.
12. Headington JT. Transverse microscopic anatomy of human scalp. Arch Dermatol 1984; 120: 449–456.
13. Whiting DA. The value of horizontal sections of scalp biopsies. J Cut Aging Cosm Dermatol 1990; 1:165–173.
14. Whiting DA. Diagnostic and predictive value of horizontal sections of scalp biopsy specimens in male pattern androgenetic alopecia. J Am Acad Dermatol 1993; 28:755–763.
15. Van Scott EJ, Reinerston RP, Steinmuller R. The growing hair roots of human scalp and morphologic changes therein following amethopterin-therapy. J Invest Dermatol 1957; 29: 197–204.
16. Guarrera M, Semino MT, Rebora A. Quantitating hair loss in women: a critical approach. Dermatology 1997; 194:12–16.
17. Rushton DH. Chemical and morphological properties of scalp hair in normal and abnormal states. Ph. D. thesis, University of Wales, United Kingdom, 1988.
18. Rushton DH, de Brouwer B, De Coster W, Van Neste DJJ. Comparative evaluation of scalp hair by phototrichogram and unit area trichogram analysis within the same subjects. Acta Dermato Venereologica 1993; 73:150–153.
19. Camacho F, Montagna W. Current concept and classification. Male androgenetic alopecia. In: Camacho F, Montagna W, eds. Trichology. Madrid: Aula Medica Group, 1997: 325–342.
20. Ludwig E, Montagna W, Camacho F. Female androgenetic alopecia. In: Camacho F, Montagna W, eds. Trichology. Madrid: Aula Medica Group, 1997: 343–355.
21. Canfield D. Photographic documentation of hair growth in androgenetic alopecia. Dermatol Clin 1996; 14:713–721.
22. Kullavanijaya P, Gritiyarangsan P, Bisalbutra P, Kulthanan R, Cardin CW. Absence of effects of dimethicone and non-dimethicone containing shampoos on daily hair loss rates. J Soc Cosmet Chem 1992; 43:195–206.

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016

23. Price VH, Menefee E. Quantitative estimation of hair growth. 1. Androgenetic alopecia in women: effect of minoxidil. J Invest Dermatol 1990; 95:683–687.
24. Price VH, Menefee E. Quantitative estimation of hair growth: comparative changes in weight and hair count with 5% and 2% minoxidil, placebo and no treatment. In: Van Neste D, Randall VA, eds. Hair Research for the Next Millenium. Amsterdam: Elsevier, 1996: 67–71.
25. Courtois M. The phototrichogram. In: Baran R, Maibach HI, eds. Cosmetic Dermatology. London: Martin Dunitz, 1994:397–400.
26. Barth JH. Measurement of hair growth. Clin Exp Dermatol 1986; 11:127–138.
27. Friedel J, Will F, Grosshans E. Le phototrichogramme. Adaptation, standardisation et application. Ann Dermatol Vénéréol 1989; 116:629–636.
28. Van Neste DJJ, de Brouwer B, De Coster W. The phototrichogram: analysis of some factors of variation. Skin Pharmacology 1994; 7:67–72.
29. Van Neste D, Dumortier M, de Brouwer B, De Coster W. Scalp immersion proxigraphy (SIP): an improved imaging technique for phototrichogram analysis. J Eur Acad Dermatol Venereol 1992; 1:187–191.
30. Hayashi S, Miayamoto I, Takeda K. Measurement of human hair growth by optical microscopy and image analysis. Brit J Dermatol 1991; 125:123–129.
31. Bouhanna P. Le tractiophototrichogramme, méthode d'appréciation objective d'une chute de cheveux. Ann Dermatol Venereol 1988; 115:759–764.

Marcel Dekker, Inc.
270 Madison Avenue, New York, New York 10016