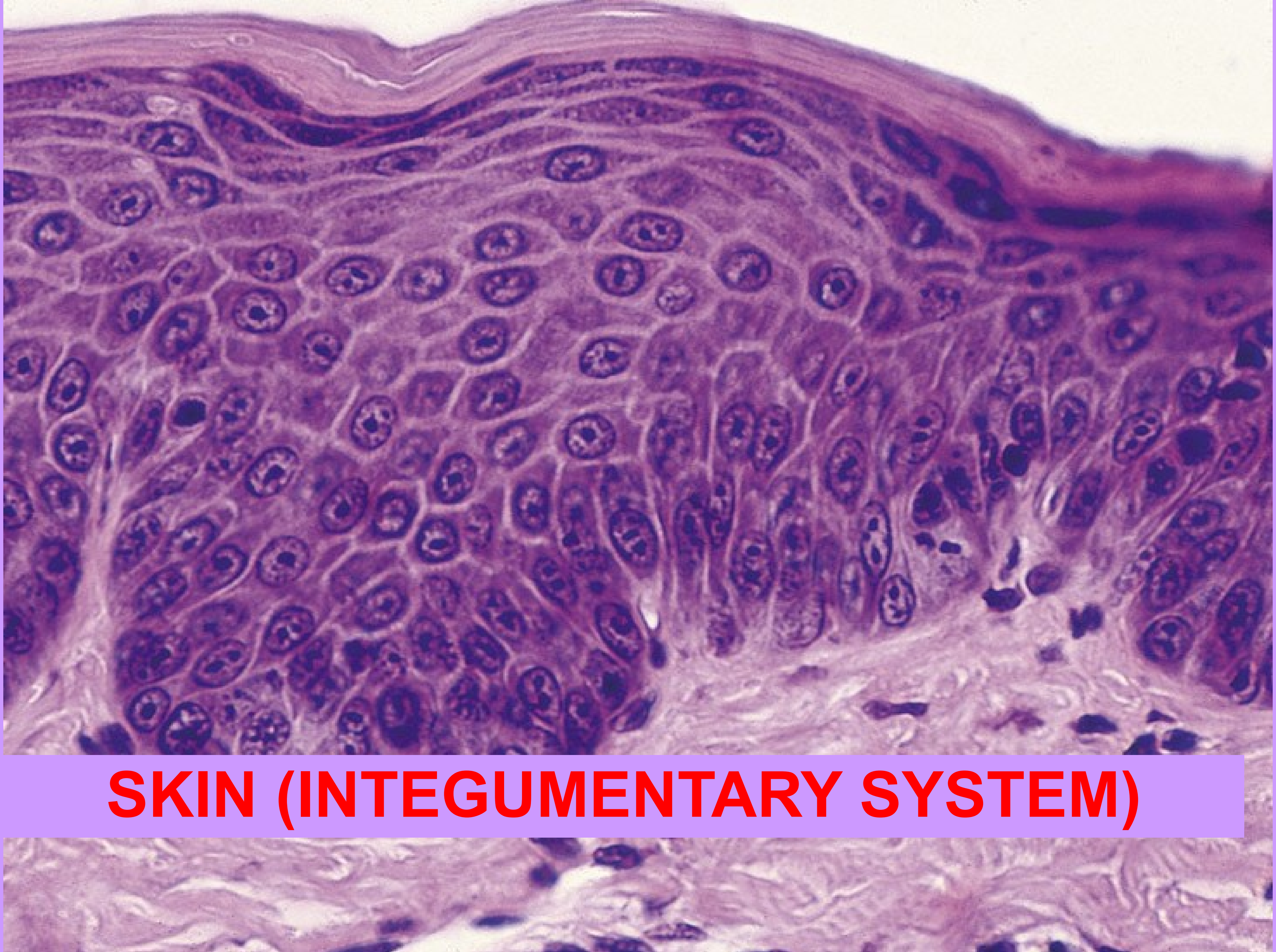


SKIN (INTEGUMENTARY SYSTEM)

SKIN

SKIN (INTEGUMENTARY SYSTEM)

Skin – the largest organ of the body, 15-20 % of total body weight, area 1,5-2 m^2

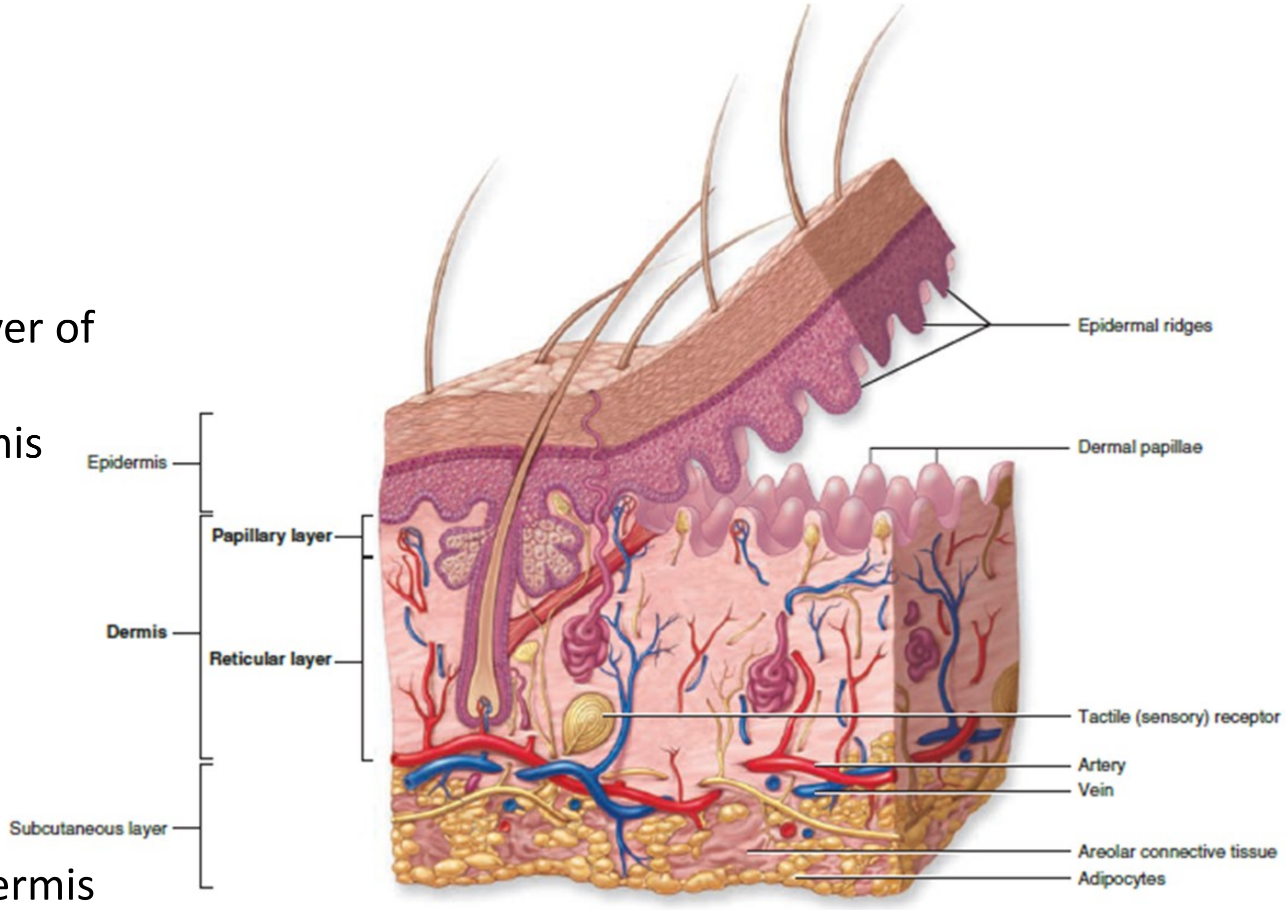
FUNCTIONS OF SKIN

- Barier protecting against physical abrasion, chemical irritants, pathogens, UV radiation, and desiccation
- Prevents water entry and loss
- Thermoregulation
- Reception of pressure and touch sensations
- Production of vitamin D
- Excretion (glands)

SKIN

COMPONENTS OF SKIN

- **Epidermis.** Stratified squamous keratinized epithelium
- **Dermis.** Composed of two layers of connective tissue containing blood vessels, nerves, sensory receptors, and sweat and sebaceous glands. Beneath the dermis is a layer of loose connective and adipose tissues that forms the superficial fascia of gross anatomy termed the hypodermis (subcutis). This layer is considered along with the skin, though technically it is not part of the integument.



Epidermal-dermal junction

- Scalloped margin at the interface of the epidermis and dermis, formed by interdigitations of:
  - *Epidermal pegs.* Downward projections of the epidermis
  - *Dermal papillae.* Upward, finger-like protrusion of connective tissue from the dermis
- This junction strengthens the attachment of the epidermis to the underlying dermis.

SKIN

Subcutaneous tissue

- Also called hypodermis (subcutis)
- **Not** considered part of skin!
- Consists of loose connective tissue and adipose tissue, which can accumulate in large fatty deposits
- Loosely binds the skin to underlying structures
- May contain the bases of sweat glands and hair follicles
- Many sensory receptors, especially Pacinian corpuscles, are present.

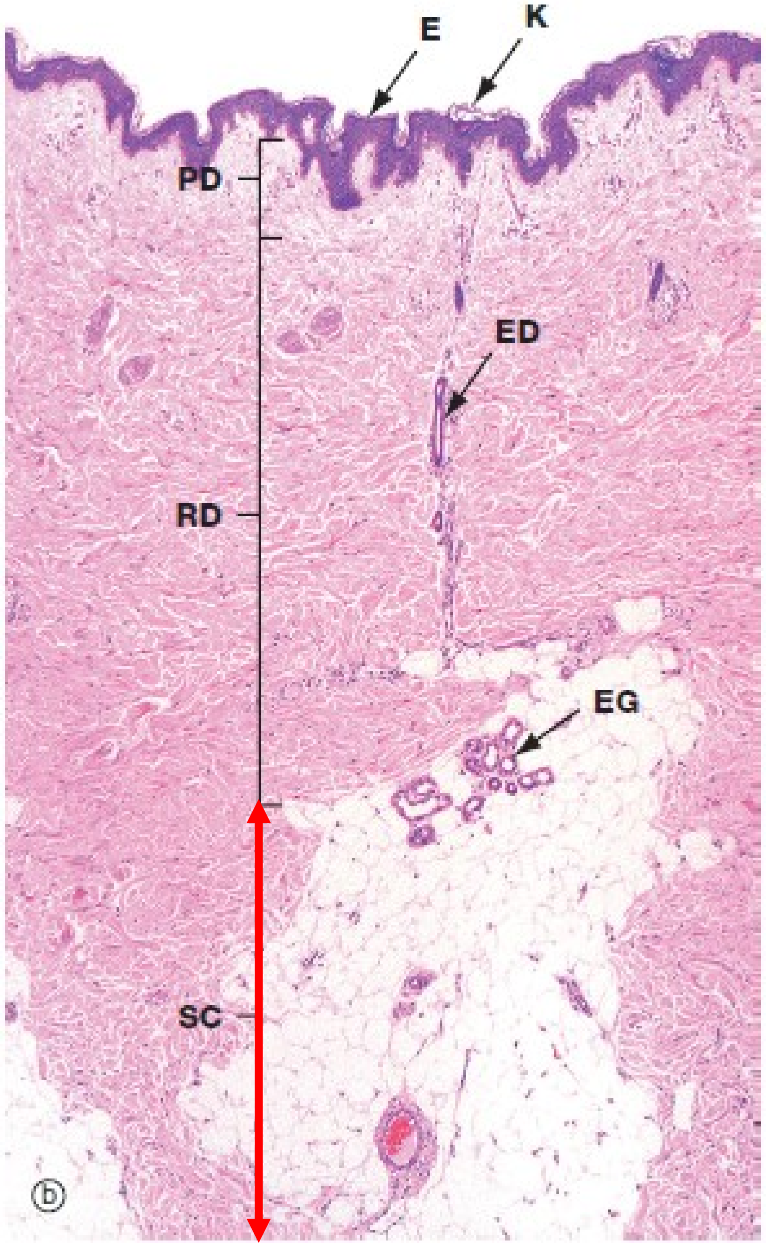


FIG. 9.1 Skin architecture
(a) Diagram (b) H&E (LP)

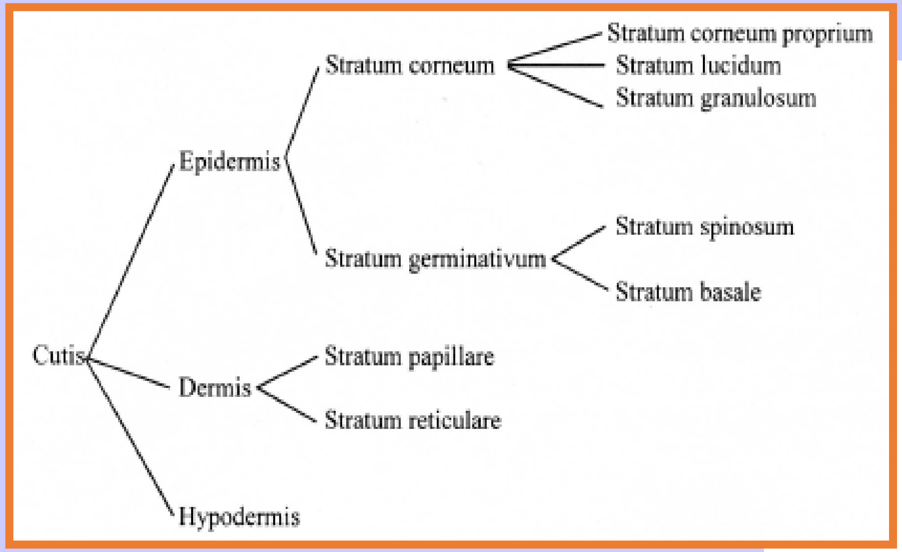
These illustrations show the basic structure of the skin, with the three component layers: *epidermis, dermis* and *subcutis*.

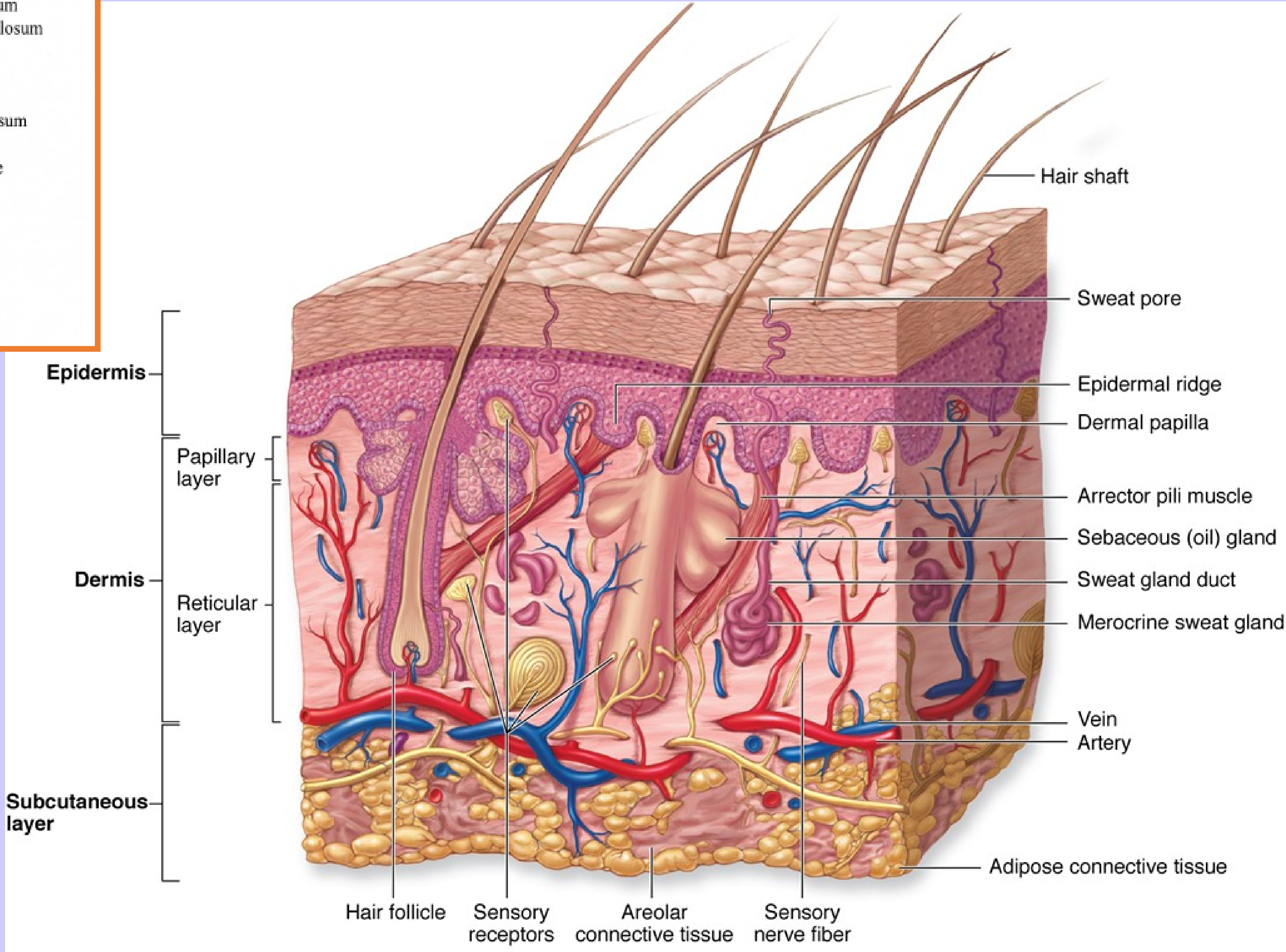
The surface layer in contact with the exterior is the epidermis E, a highly specialised self-regenerating stratified squamous epithelium which produces a non-living surface rich in a protein, *keratin* K, that is tough and protective and is also partially water resistant (see Ch. 5). The epidermis also contains non-epithelial cells: *melanocytes* produce melanin pigment to protect against UV light, *Langerhans cells* act as antigen-presenting cells and induce immune responses to new antigens and *Merkel cells* act as touch receptors. The epidermis is tightly bound to the underlying dermis by a specialised basement membrane. Additional resistance to frictional shearing force is provided by a series of epidermal downgrowths (*rete ridges*) which extend into the superficial dermis, with their papillary dermal mirror images projecting upwards (*dermal papillae*) to provide stronger tethering. These are most developed where exposure to shearing forces is almost constant (e.g. sole, palm).

The dermis immediately adjacent to the epidermis is called the *papillary dermis* PD; it has relatively fine collagen fibres and contains numerous small blood vessels, sensory nerve endings and sensory structures. The *reticular dermis* RD is the deeper tough layer of horizontally arranged collagen and elastin fibres with fibroblasts.

The deepest layer is the subcutis SC, also called the *panniculus* or *hypodermis*. It is a layer of adipose tissue often compartmentalised by fibrous septa, extending downwards from dermis to the underlying structural connective tissue fascia. The subcutis acts as a shock absorber and thermal insulator as well as a fat store.

The dermis and subcutis contain an assortment of skin *adnexa (appendages)* such as *hair follicles, sebaceous glands, eccrine (sweat) glands* EG and ducts ED and, in some areas, *apocrine glands*.


Stratum corneum proprium
Stratum corneum
Stratum lucidum
Stratum granulosum
Epidermis
Stratum spinosum
Stratum germinativum
Stratum basale
Cutis
Stratum papillare
Dermis
Stratum reticulare
Hypodermis


Hair shaft
Sweat pore
Epidermis
Epidermal ridge
Dermal papilla
Papillary layer
Arrector pili muscle
Sebaceous (oil) gland
Dermis
Sweat gland duct
Reticular layer
Merocrine sweat gland
Vein
Artery
Subcutaneous layer
Adipose connective tissue
Hair follicle
Sensory receptors
Areolar connective tissue
Sensory nerve fiber

SKIN

CLASSIFICATION OF SKIN (Based epidermal thickness)

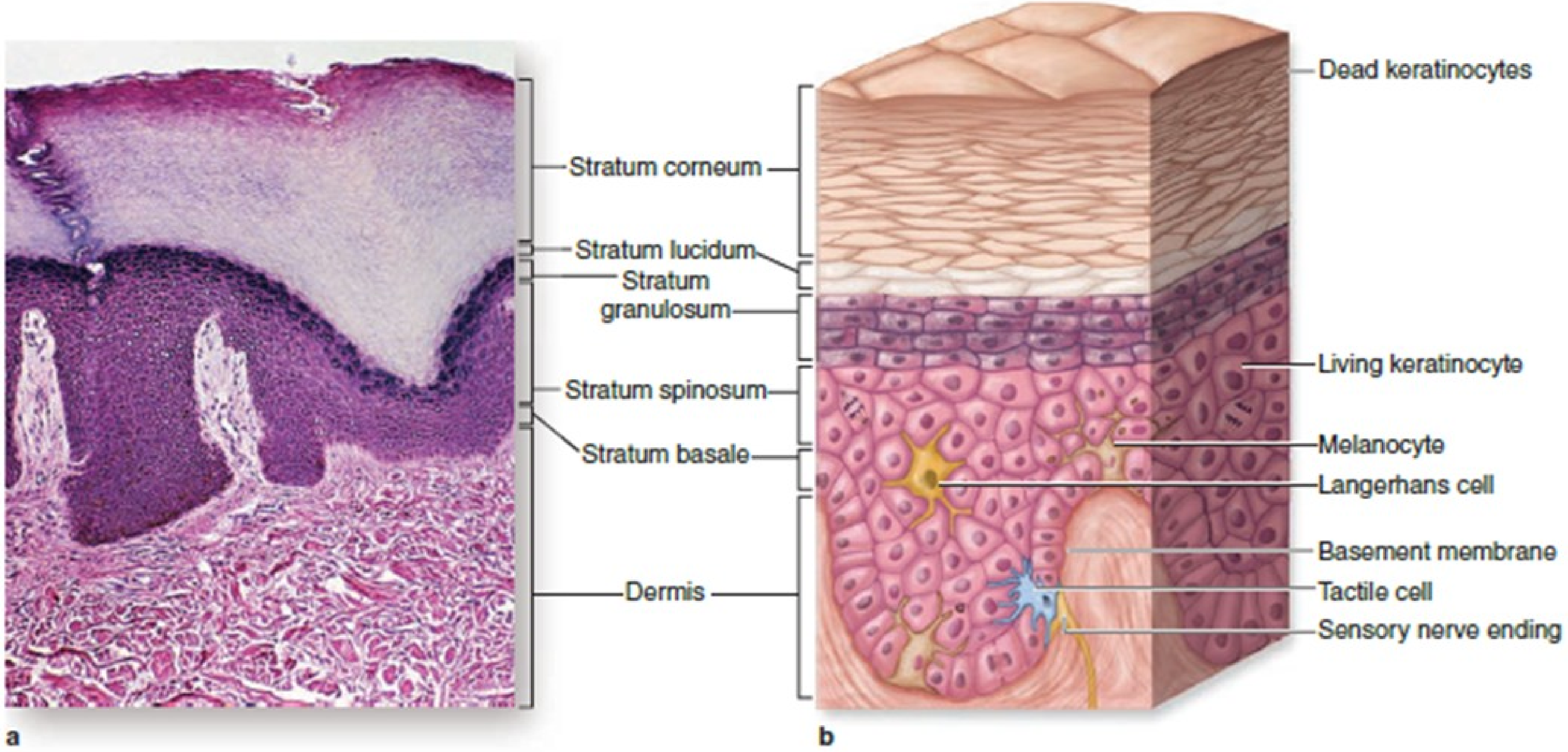
- **Thin skin**
  - Covers entire body except palms and soles; 0.5 mm thick on the eyelid, 5 mm thick on the back and shoulders
  - Epidermis is thin, 0.075-0.15 mm thick, but the dermis varies from thin to very thick, depending on location.
  - Possesses hair with sebaceous glands
  - Sweat glands are present
  - Epidermis has not stratum lucidum
  - S. granulosum and s. corneum are much thinner

The interface between dermis and epidermis in thin skin is held together firmly by interlocking epidermal ridges or pegs (**EP**) and dermal papillae (**DP**). The dermis (**D**) of thin skin is more cellular and well vascularized than that of thick skin, with elastin and less coarse bundles of collagen. The epidermis usually shows only four layers in thin skin: the one-cell thick stratum basale (**B**) containing most mitotic cells; the stratum spinosum (**S**) where synthesis of much keratin and other proteins takes place; the stratum granulosum (**G**); and the stratum corneum (**C**), consisting of dead squames composed mostly of keratin. (X240; H&E)

SKIN

CLASSIFICATION OF SKIN (Based epidermal thickness)

- **Thick skin**
  - Located on palms of the hands and soles of the feet; 0.8-1.5 mm thick
  - Epidermis is 0.4-0.6 mm thick
  - Hairless, no sebaceous glands
  - Sweat glands are present



(a) Micrograph shows the sequence of the epidermal layers in thick skin and the approximate sizes and shape of keratinocytes in these layers. Also shown are the coarse bundles of collagen in the dermis and on the far left, the duct from a sweat gland entering the epidermis from a dermal papilla and coiling to a surface pore through all the strata. (X100; H&E)

(b) Diagram illustrating the sequence of the epidermal layers also indicates the normal locations of three important nonkeratinocyte cells in the epidermis: melanocytes, a Langerhans cell, and a tactile Merkel cell.

SKIN

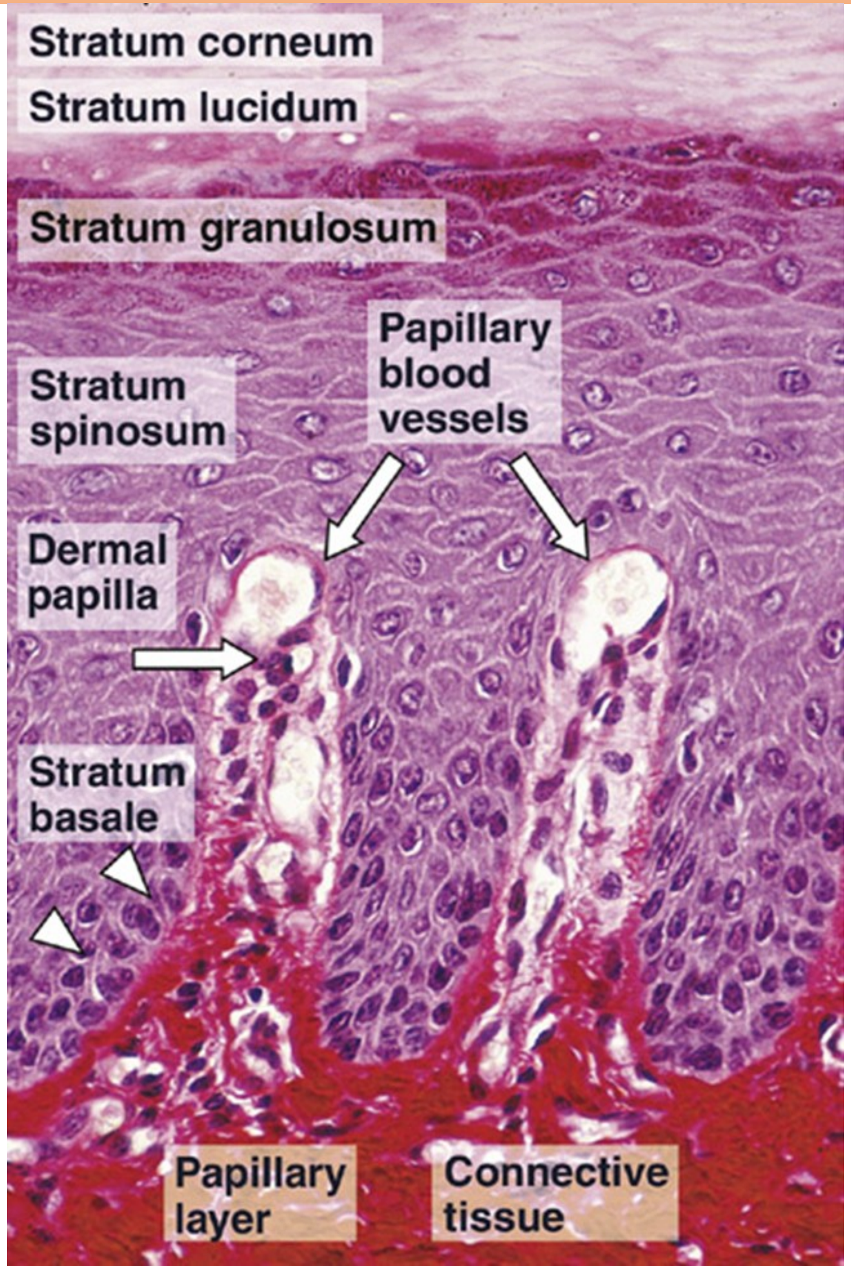
Layers of the epidermis and keratinization

The epidermis is a stratified squamous, keratinized (dry) epithelium. It is continually renewed every 15-30 days. Rapid cell proliferation occurs primarily in the deepest layer (stratum basale) and daughter cells differentiate as they migrate toward the surface. This differentiation involves a process called **keratinization**, which results in a variably thick layer of nonliving cellular husks at the surface of the epidermis. All cells in the epidermis that undergo the keratinization process are called **keratinocytes**.

Layers of the epidermis:

- *Stratum basale* (germinativum)

  A single layer of cuboidal to columnar shaped cells (keratinocytes) that rest on the basement membrane and undergo rapid cell proliferation. These cells contain intermediate filaments composed of cytokeratin (keratin proteins) (tonofilaments).



SKIN

Layers of the epidermis:

- *Stratum spinosum*

  Spiny cell layer; 3-10 cells thick. This layer is so-called because the cells are attached to one another by desmosomes, and the cellular shrinkage resulting from fixation produces the spine-like structures. These cells accumulate bundles of tonofilaments called **tonofibrils**.

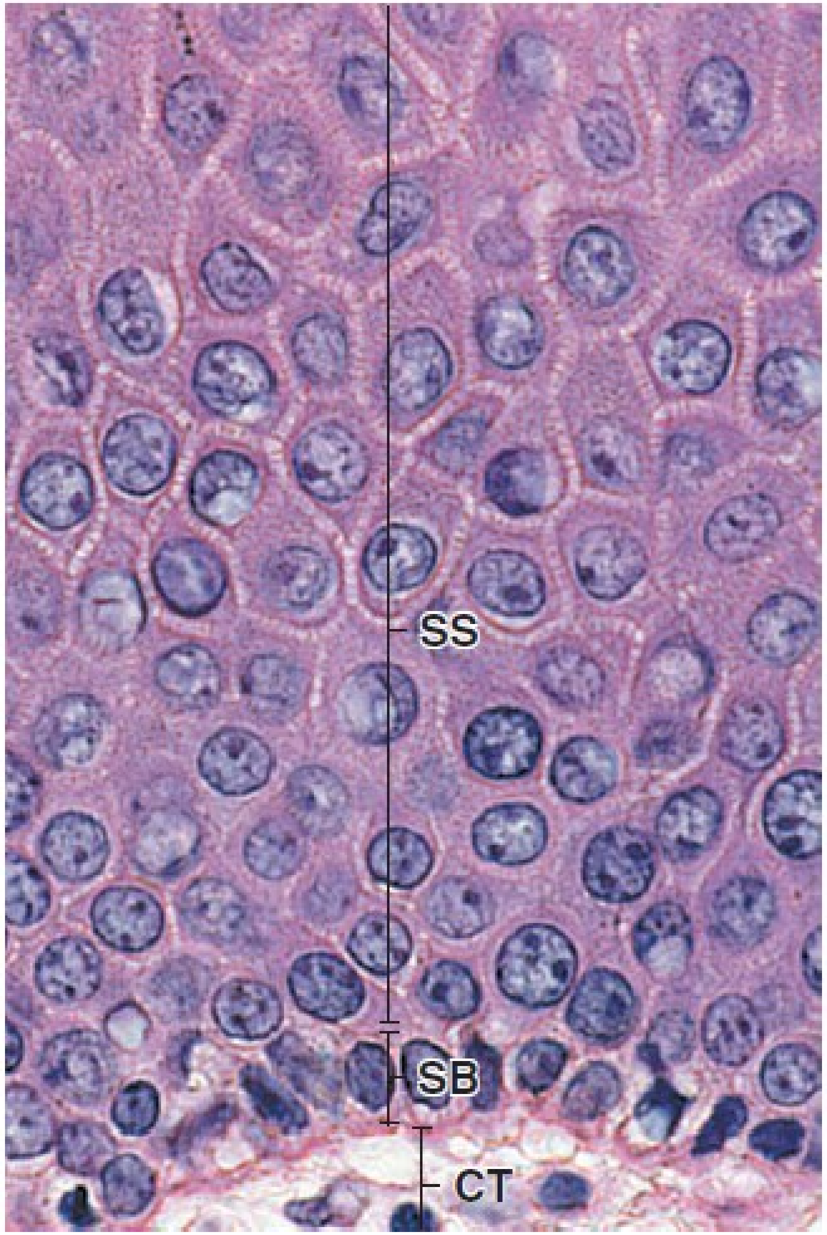
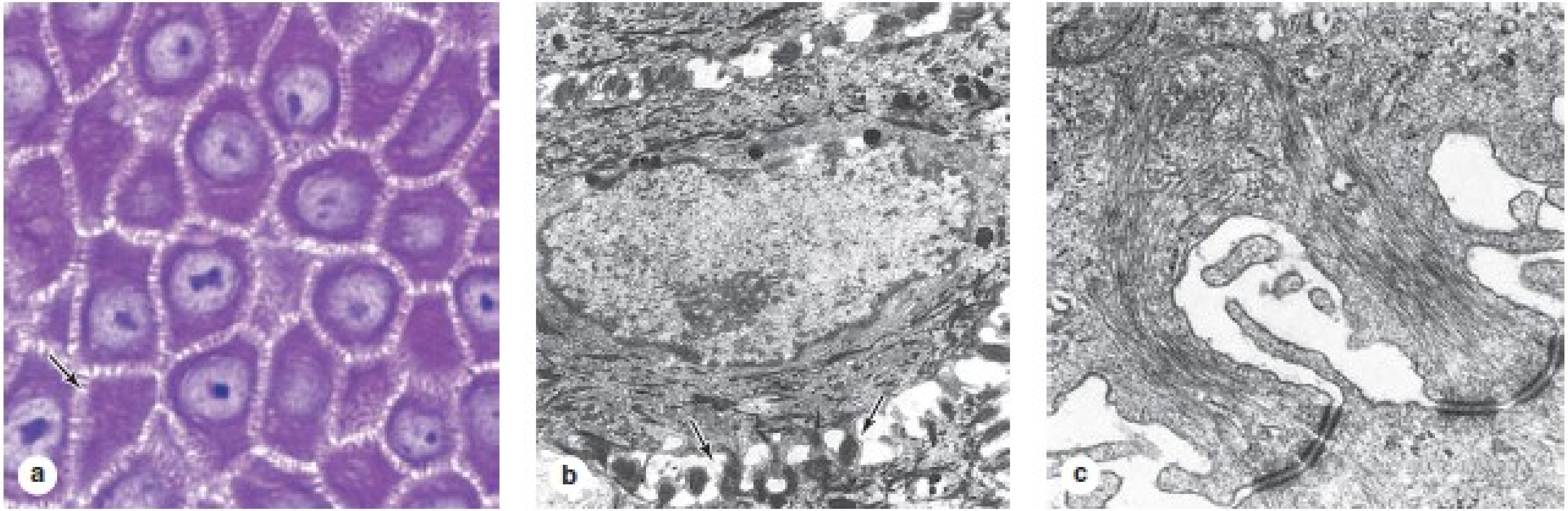


FIGURE 15.3 ▲ Photomicrograph of the stratum spinosum and stratum basale. The epidermis of thin skin is shown here at higher magnification. The one-cell-deep layer at the base of the epidermis just above the connective tissue (*CT*) of the dermis is the stratum basale (*SB*). The cells of this layer rest on the basement membrane. A layer referred to as the *stratum spinosum* (*SS*) is located just above the stratum basale. It consists of cells with spinous processes on their surfaces. These processes are attached to spinous processes of neighboring cells by desmosomes and together appear as intercellular bridges. ×640.

FIGURE 18–4 Keratinocytes of the stratum spinosum.



(a) A section of epidermal stratum spinosum of thick skin, showing cells with numerous short cytoplasmic projections (**arrow**). (X400; PT)

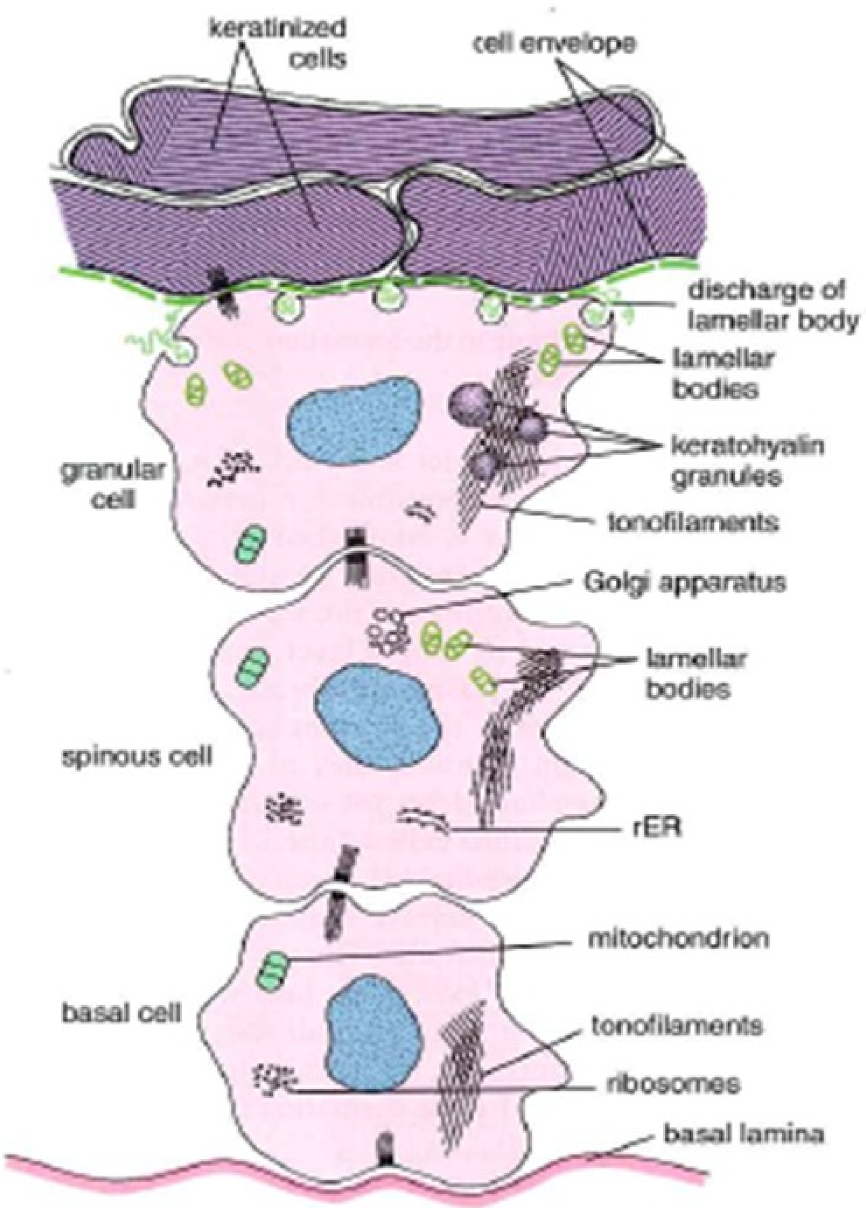
(b) TEM of a single spinous keratinocyte with surface projections (**arrows**). (8400)

(c) Detail of the desmosomes joining two cells showing intermediate filaments associated with desmosomes. (X40,000)

SKIN

Layers of the epidermis:

- *Stratum granulosum*
  - two to four cells thick
  - cells synthesize basophilic, keratohyalin granules, which associate with the tonofibrils
  - Cells also accumulate lamellar bodies, which contain a lipid material that is secreted and serves as a sealant and penetration barrier between cells.
  - Cells also begin to lose other organelles.



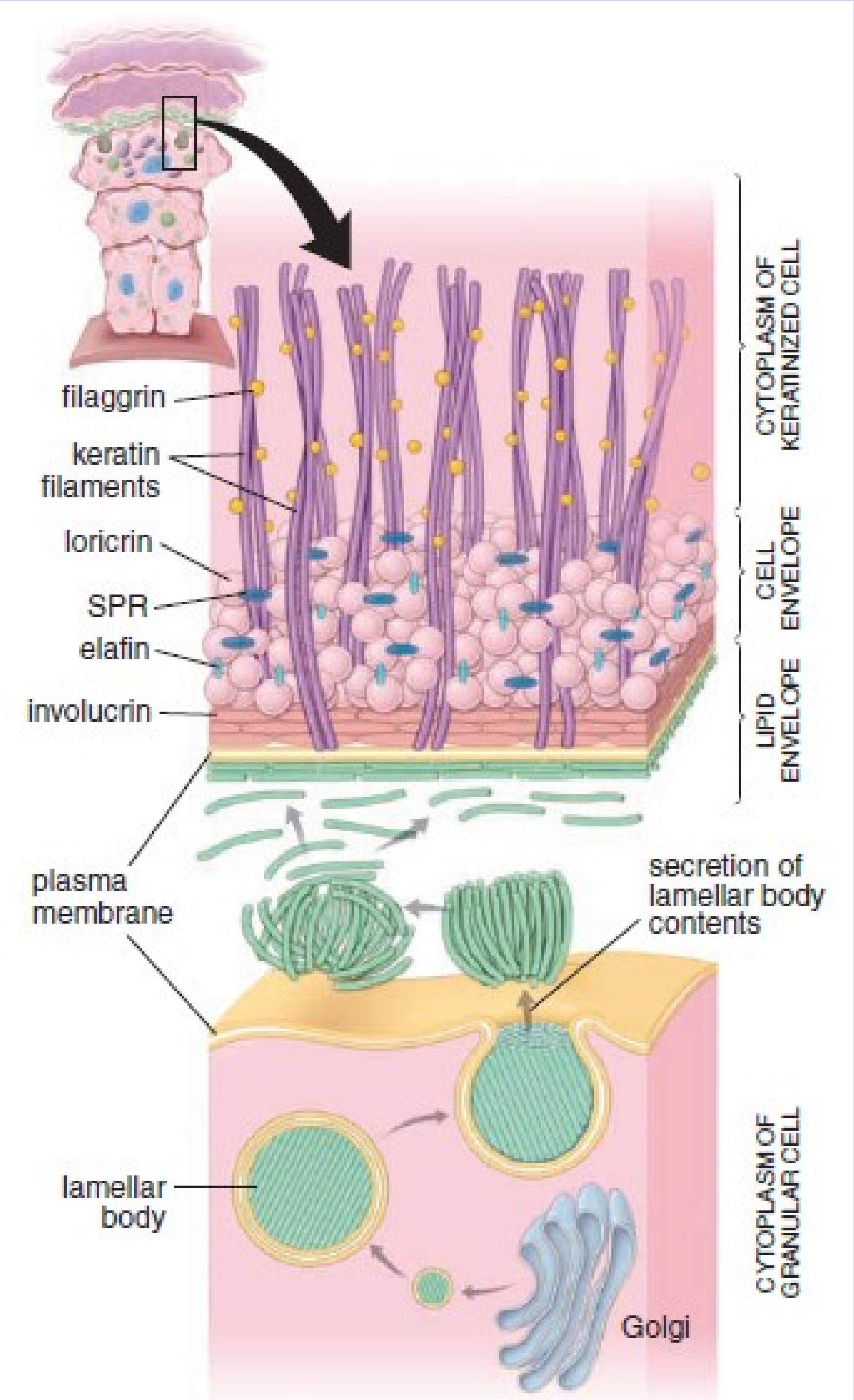


FIGURE 15.5 ▲ Schematic diagram of the epidermal water barrier. The heterogeneous mixture of glycosphingolipids, phospholipids, and ceramides makes up the lamellae of the lamellar bodies. The lamellar bodies, produced within the Golgi apparatus, are secreted by exocytosis into the intercellular spaces between the stratum granulosum and stratum corneum, where they form the lipid envelope. The lamellar arrangement of lipid molecules is depicted in the intercellular space just below the thickened plasma membrane and forms the cell envelope of the keratinized keratinocyte. The innermost part of the cell envelope consists primarily of loricrin molecules (*pink spheres*) that are cross-linked by small proline-rich (*SPR*) proteins and elafin. The layer adjacent to the cytoplasmic surface of the plasma membrane consists of the two tightly packed proteins involucrin and cystatin α. Keratin filaments (tonofilaments) bound by filaggrin are anchored into the cell envelope.

SKIN

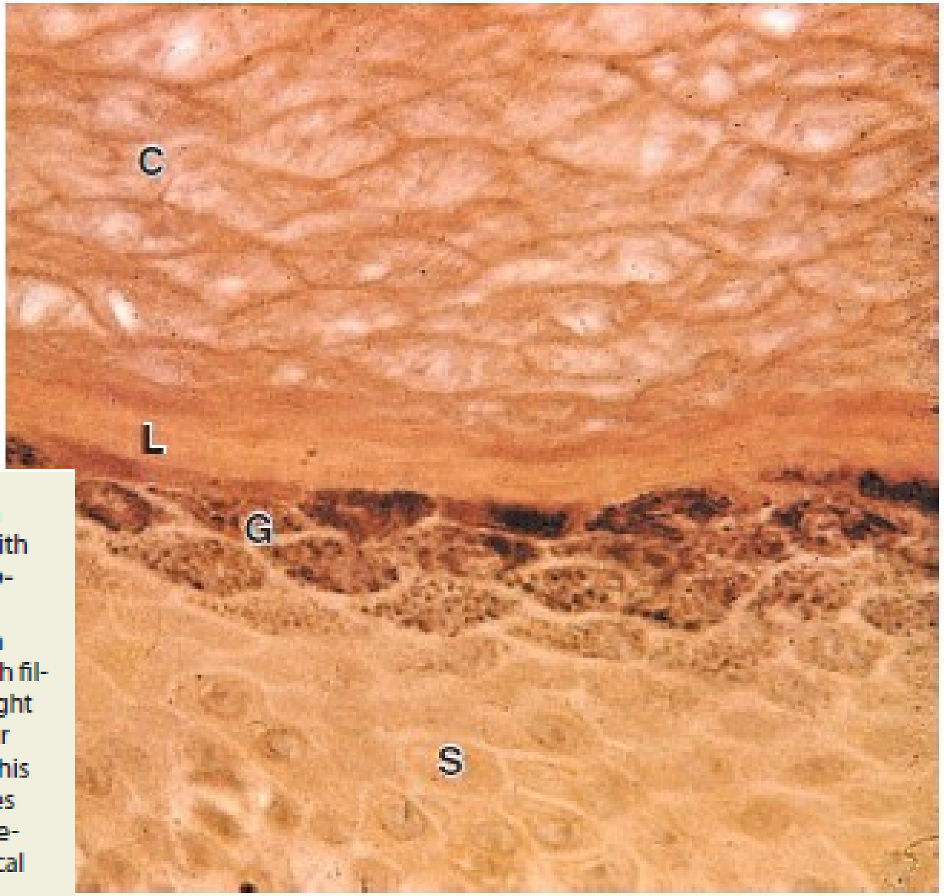
Layers of the epidermis:

- *Stratum lucidum*

  A clear layer of non-nucleated, flattened cells that is only visible as a distinct layer in thick skin. In this region, the proteins contained in the keratohyalin granules mediate the aggregation of tonofibrils. This process occurs whether or not a distinct stratum lucidum is visible.

- *Stratum corneum*

  Variably thick layer of extremely flattened, cornified scales containing aggregated tonofibrils surrounded by a thickened plasma membrane. These cell remnants are sloughed off without damage to the underlying, living epidermal cells.



In keratinocytes moving upward from the stratum spinosum (**S**), differentiation proceeds with the cells becoming filled with numerous large, amorphous masses of protein called **keratohyaline granules**.

Cells with these basophilic granules make up the stratum granulosum (**G**), where keratin filaments are cross-linked with filaggrin and other proteins from these granules to produce tight bundles filling the cytoplasm and flattening the cells. Smaller organelles called **lamellar granules** undergo exocytosis in this layer, secreting a lipid-rich layer around the cells which makes the epidermis impermeable to water. Together, the lipid envelope and the keratin-filled cells determine most of the physical properties of the epidermis.

The cells leaving the stratum granulosum, still bound together by desmosomes, undergo terminal differentiation and in thick skin appear as a dense, thin layer called the **stratum lucidum** (**L**). Here proteins are dispersed through the tonofibril bundles, giving this layer a regular, "clear" appearance. In the most superficial stratum corneum (**C**), the cells have lost nuclei and cytoplasm, consisting only of flattened, keratinized structures called **squames** bound by hydrophobic, lipid-rich intercellular cement. At the surface they are worn away (thick skin) or flake off (thin skin). (X560; H&E)

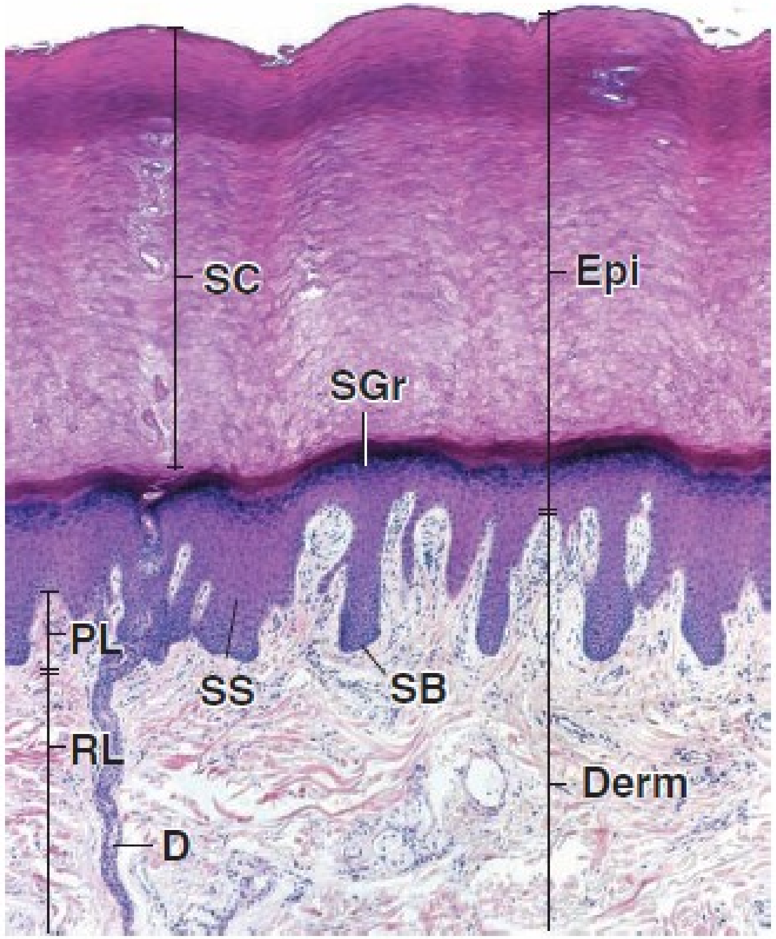
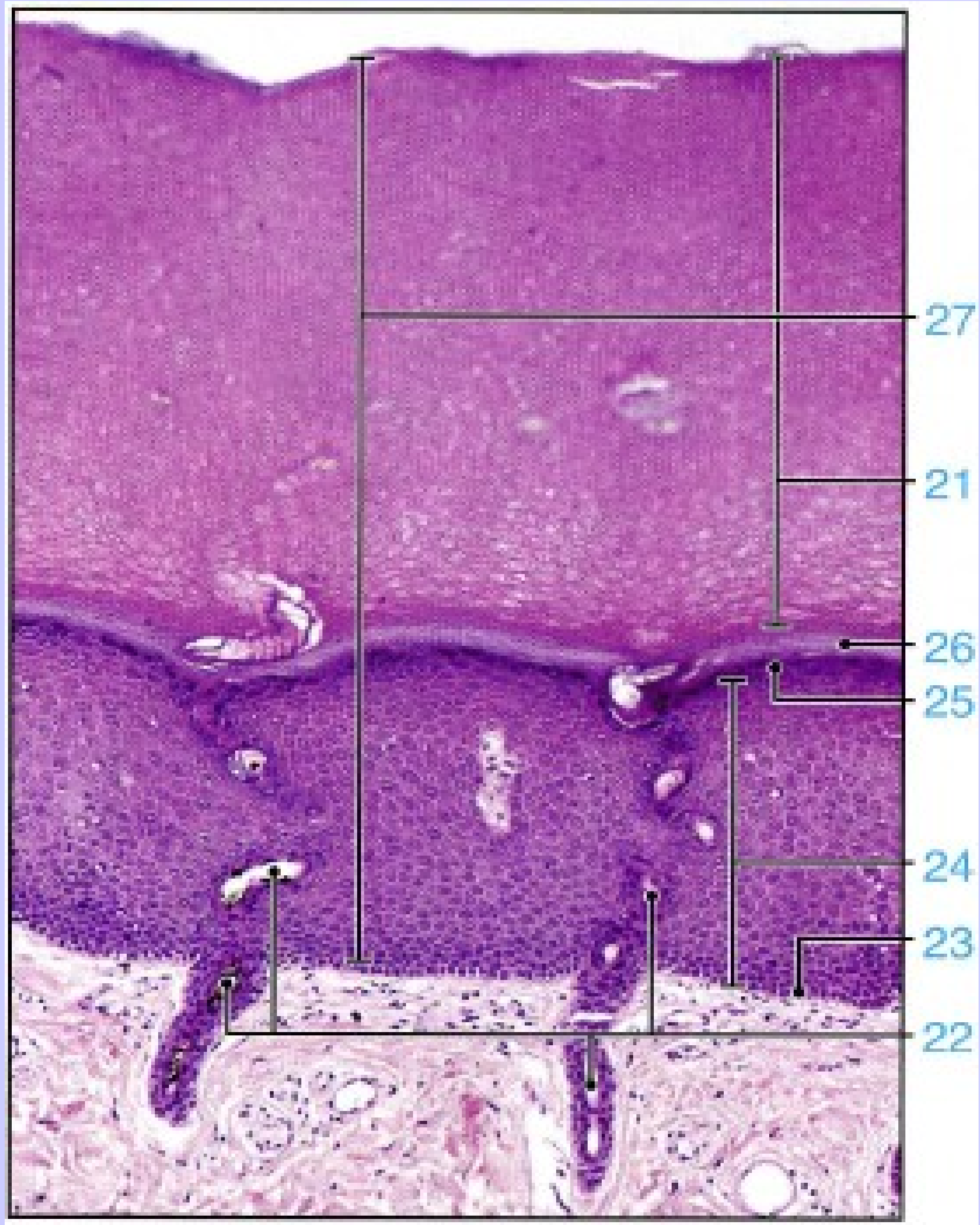


FIGURE 15.2 ▲ Photomicrograph showing the layers of thick skin. This specimen obtained from the skin of the sole of the foot (human) shows epidermis (*Epi*) containing the extremely thick stratum corneum (*SC*). Remaining layers of the epidermis (except for the stratum lucidum, which is not present on this slide)—that is, the stratum basale (*SB*), the stratum spinosum (*SS*), and the stratum granulosum (*SGr*)—are clearly visible in this routine H&E preparation. The duct of a sweat gland (*D*) can be seen on the *left* as it traverses the dermis (*Derm*) and further spirals through the epidermis. At the sites where the ducts of the sweat gland enter the epidermis, note the epidermal downgrowths known as *interpapillary pegs*. The dermis contains papillae, protrusions of connective tissue that lie between the interpapillary pegs. Note also the greater cellularity of the papillary layer (*PL*) and that the collagen fibers of the reticular layer (*RL*) are thicker than those of the papillary layer. ×65.



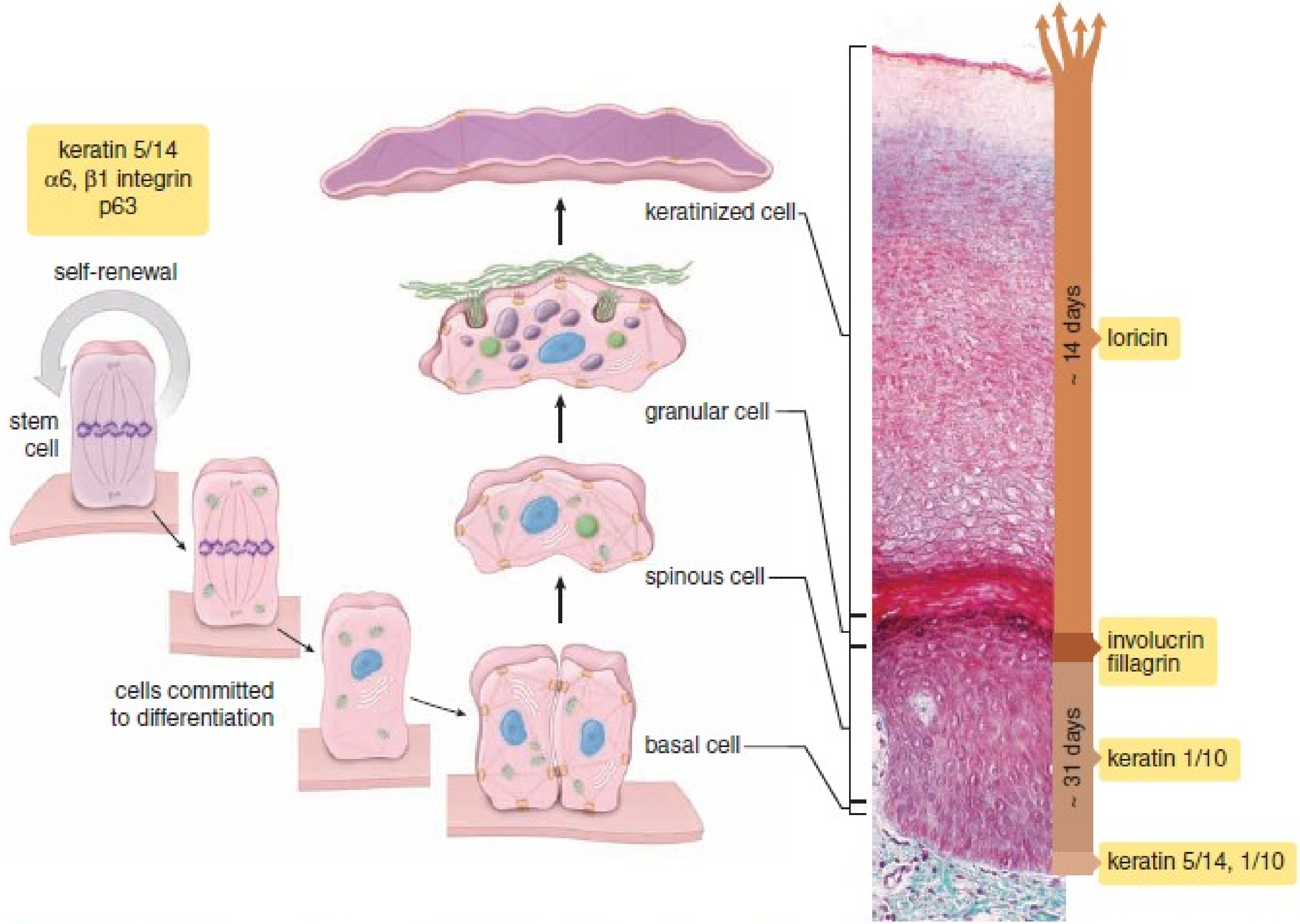


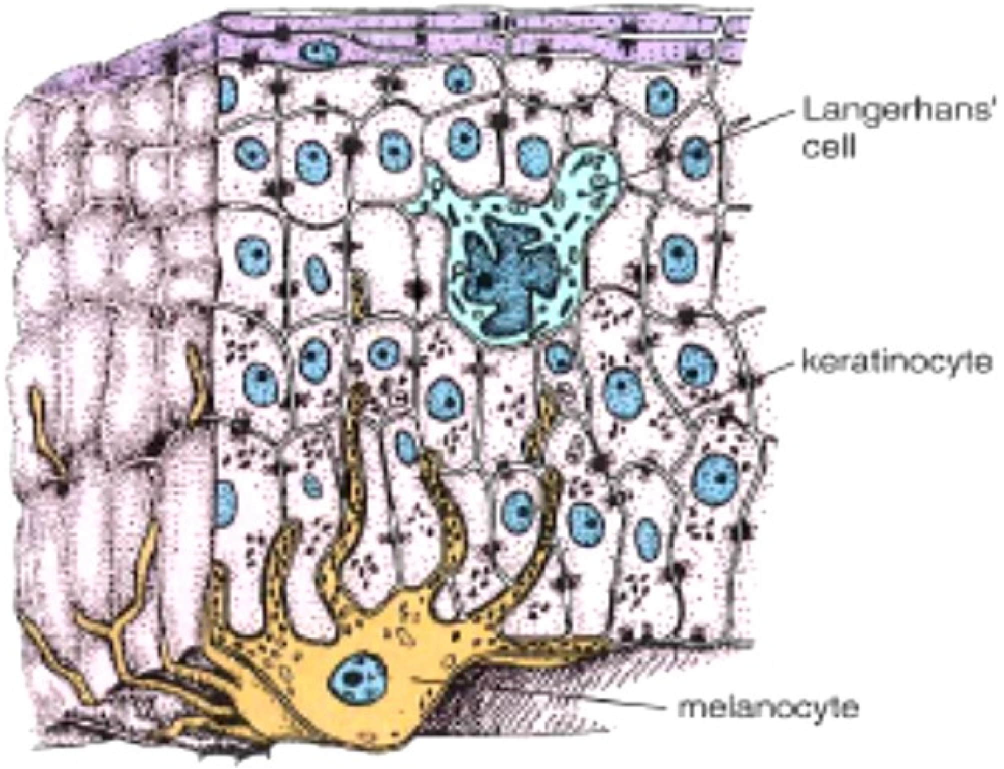
FIGURE 15.7 ▲ Schematic diagram of epidermal cell differentiation and replacement. Epidermal cell replacement is initiated by the division of stem cells in the stratum basale. Newly formed cells further undergo divisions in the stratum basale and move upward as they differentiate into keratinized cells, which eventually are lost by exfoliation on the skin surface. To maintain this equilibrium between cell divisions and cell loss at the skin surface, each cell has a predetermined time to travel through specific compartments of the epidermis and to perform specific functions. Mitotic divisions in the stratum basale take about 1 to 2 days; after that, it takes an average 31 days for keratinocytes to move through the stratum spinosum (spinous cells) and differentiate into granular cells in the stratum granulosum. It takes an additional 14 days for the keratinized cell to cross the stratum corneum (assuming an average thickness of 16 to 20 cells in humans). Therefore, the total epidermal turnover time is approximately 47 days. At every stage of differentiation, cells express different molecular markers (see *yellow boxes*), which can be useful in identifying specific cells using immunocytochemical methods. *Inset* on the *left* shows full-thickness section of the epidermis from a human fingertip stained with Mallory's trichrome. ×260.

SKIN

EPIDERMIS

Cell types:

- *Keratinocytes*
  - Keratinizing epidermal cells, major cell type in the epidermis
  - Function is to produce intermediate filaments composed of keratins
  - Amout of keratin filaments increases as the cells move upword
- *Melanocytes*
- *Langerhans cells*
- *Merkel's cells*



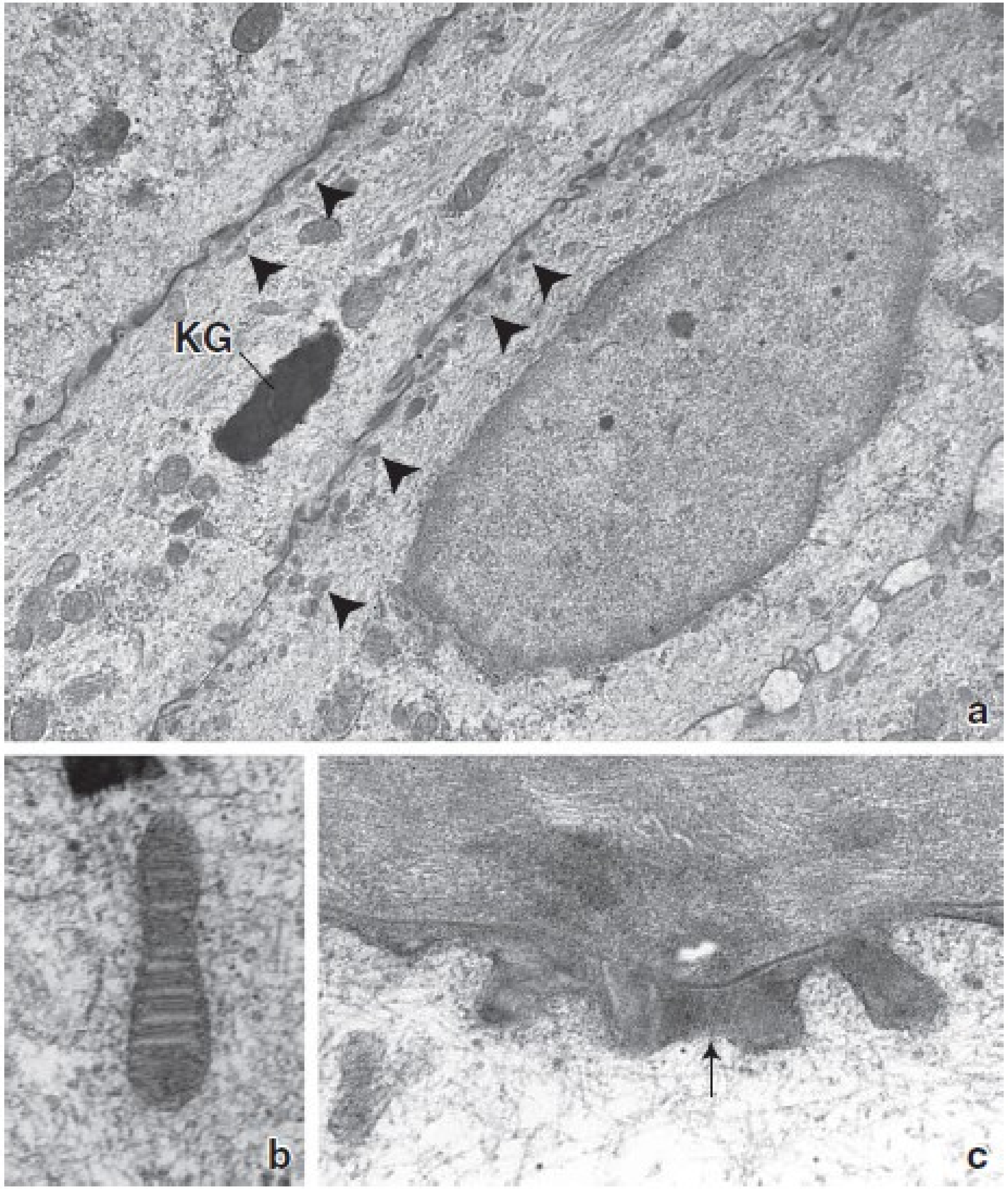


FIGURE 15.6 ▲ Electron micrographs of keratinocytes. a. Much of the keratinocyte cytoplasm is filled with tonofilaments. One keratinocyte exhibits a keratohyalin granule (*KG*). Near the plasma membrane closest to the surface (*upper left*), two keratinocytes display lamellar bodies (*arrowheads*). ×8,500. **b.** A lamellar body at higher magnification. ×135,000. **c.** Part of a keratinized cell and the underlying keratinocyte. Located between the cells are the contents of the lamellar bodies, which have been discharged into the intercellular space (*arrow*) to form the lipid envelope. ×90,000. (Courtesy of Dr. Albert I. Farbman.)

SKIN

EPIDERMIS

Cell types:

- *Keratinocytes*
- *Melanocytes*. Melanin pigment-producing cells
  - Present in stratum basale and stratum spinosum
  - Rounded cell bodies with clear cytoplasm. Numerous "dendrite-like" processes insinuate themselves between the keratinocytes
  - Synthesize melanin, a dark brown pigment that is packaged into melanosomes and injected into keratinocytes
  - Melanin caps the keratinocyte nucleus, reducing damage from solar radiation.
- *Langerhans cells*
- *Merkel's cells*

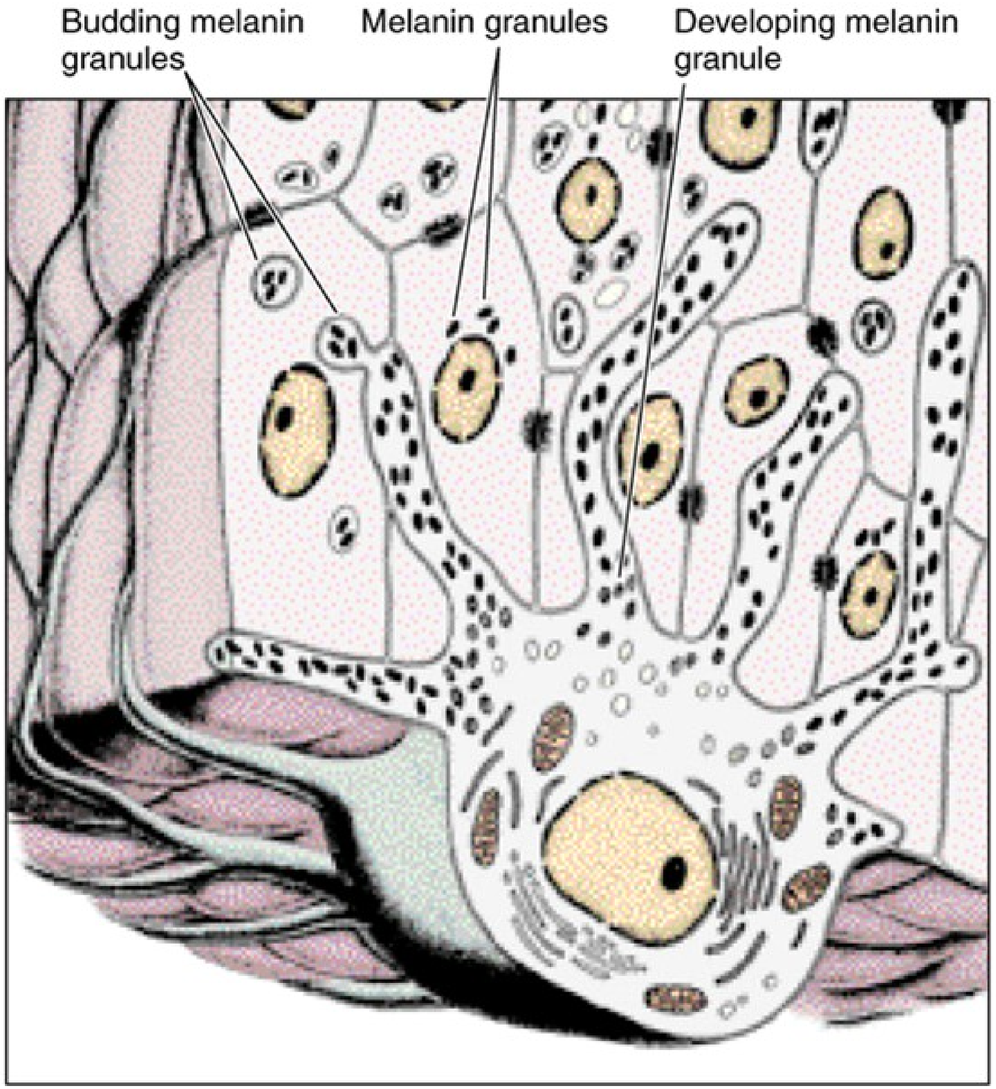
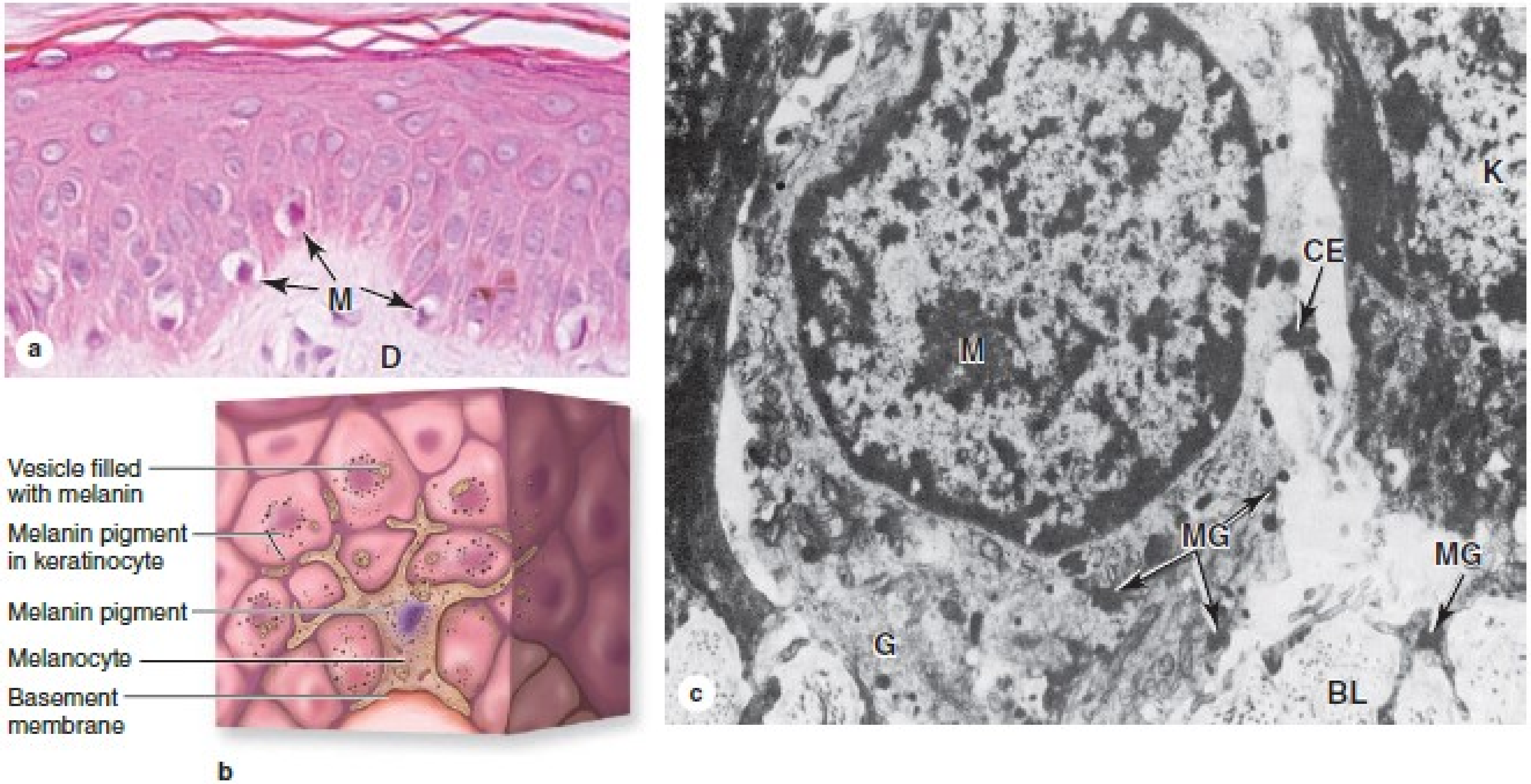


FIGURE 18–6 **Melanocytes.**



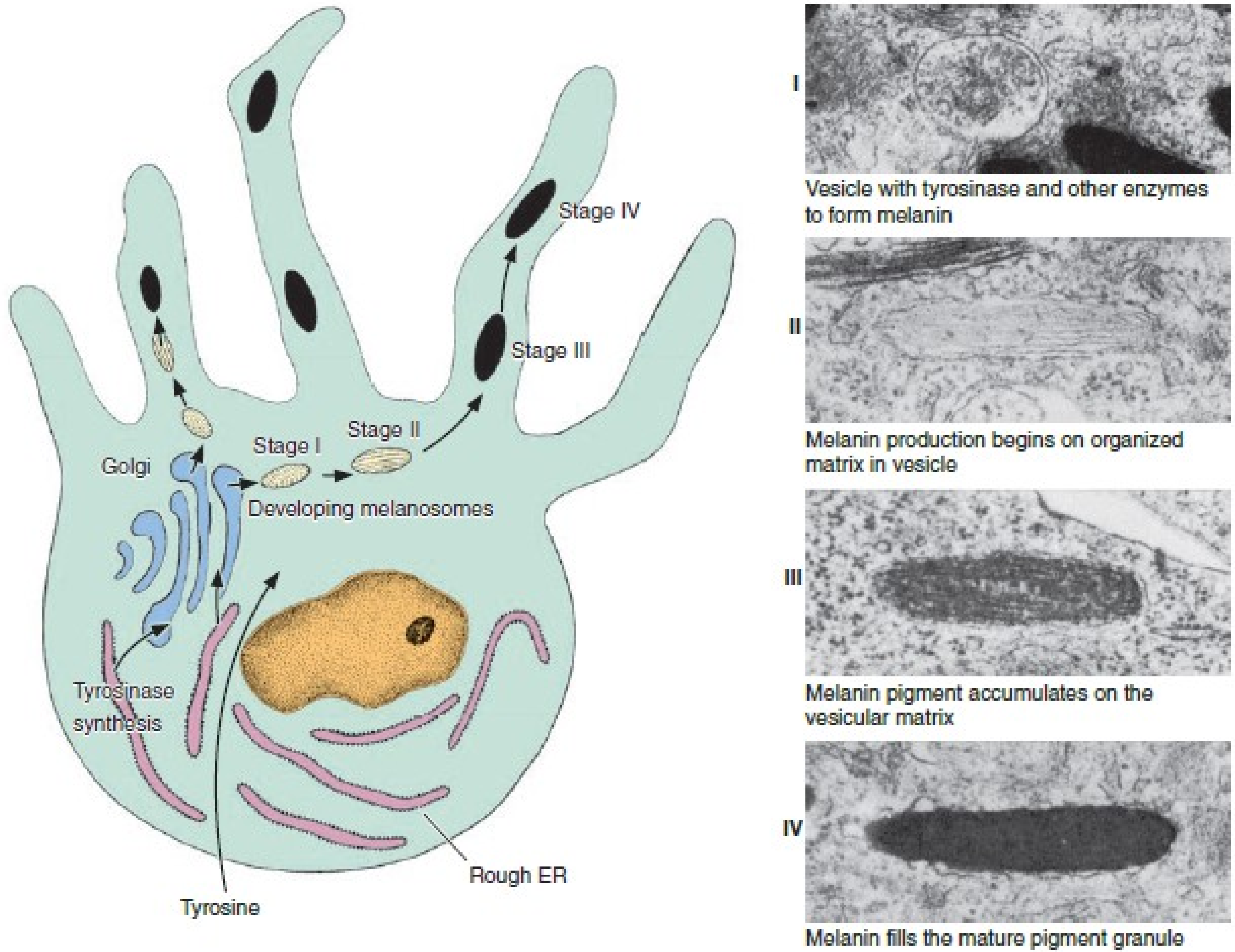
Melanocytes are located in the epidermal basal layer and synthesize **melanin granules** and transfer them into neighboring **keratinocytes**. Transfer occurs through many long, branching melanocyte processes that extend into the spinous layer and are not seen in routine microscopy.

(a) In light microscopy melanocytes (**M**) typically appear as rounded, pale-staining or clear cells just above the dermis (**D**). Melanocytes are difficult to distinguish from Merkel cells by routine microscopy. Langerhans cells are also rounded, poorly stained cells but are typically located more superficially than melanocytes, in the stratum spinosum. (X400; H&E)

(b) Diagram of a melanocyte shows the irregular cytoplasmic processes between neighboring keratinocytes for transfer of melanin to those cells.

(c) Ultrastructurally, a melanocyte is located on the basal lamina (**BL**) and has well-developed Golgi complexes (**G**) producing the vesicles in which melanin is synthesized. As they fill, these vesicles become melanin granules (**MG**), which accumulate at the tips of the dendritic cytoplasmic extensions (**CE**) before transfer to keratinocytes (**K**). (X14,000)

FIGURE 18–7 Melanosome formation.



The diagram of a melanocyte shows the main features of melanin formation. The granules containing melanin mature through four stages that are characterized ultrastructurally, as shown on the right. **Tyrosinase** is synthesized in the rough ER, processed through the Golgi apparatus, and accumulates in vesicles that also have a fine granular matrix of other proteins (**stage I** melanosomes). Melanin synthesis begins in the ovoid **stage II** melanosomes, in which the matrix has been organized into parallel filaments on which polymerized melanin is deposited and accumulates in **stage III**. A mature melanin granule (**stage IV**) has lost tyrosinase and other activities and has the internal matrix completely filled with melanin. The mature granules are ellipsoid, approximately 0.5 by 1 μm in size, and visible by light microscopy.

Melanin granules are transported to the tips of the processes of melanocyte and are then transferred to the neighboring keratinocytes of the basal and spinous layers. In keratinocytes the melanin granules are transported to a region near the nucleus, where they accumulate as a supranuclear cap shading the DNA against the harmful effects of UV radiation.

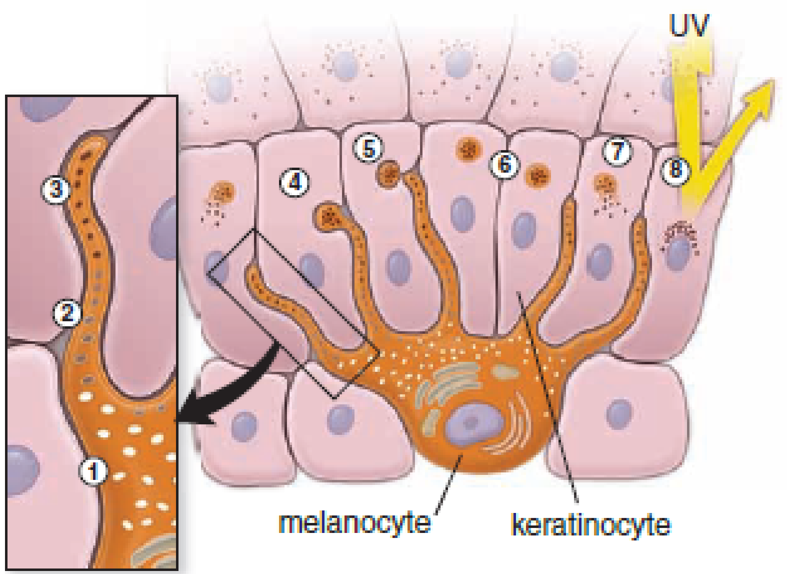
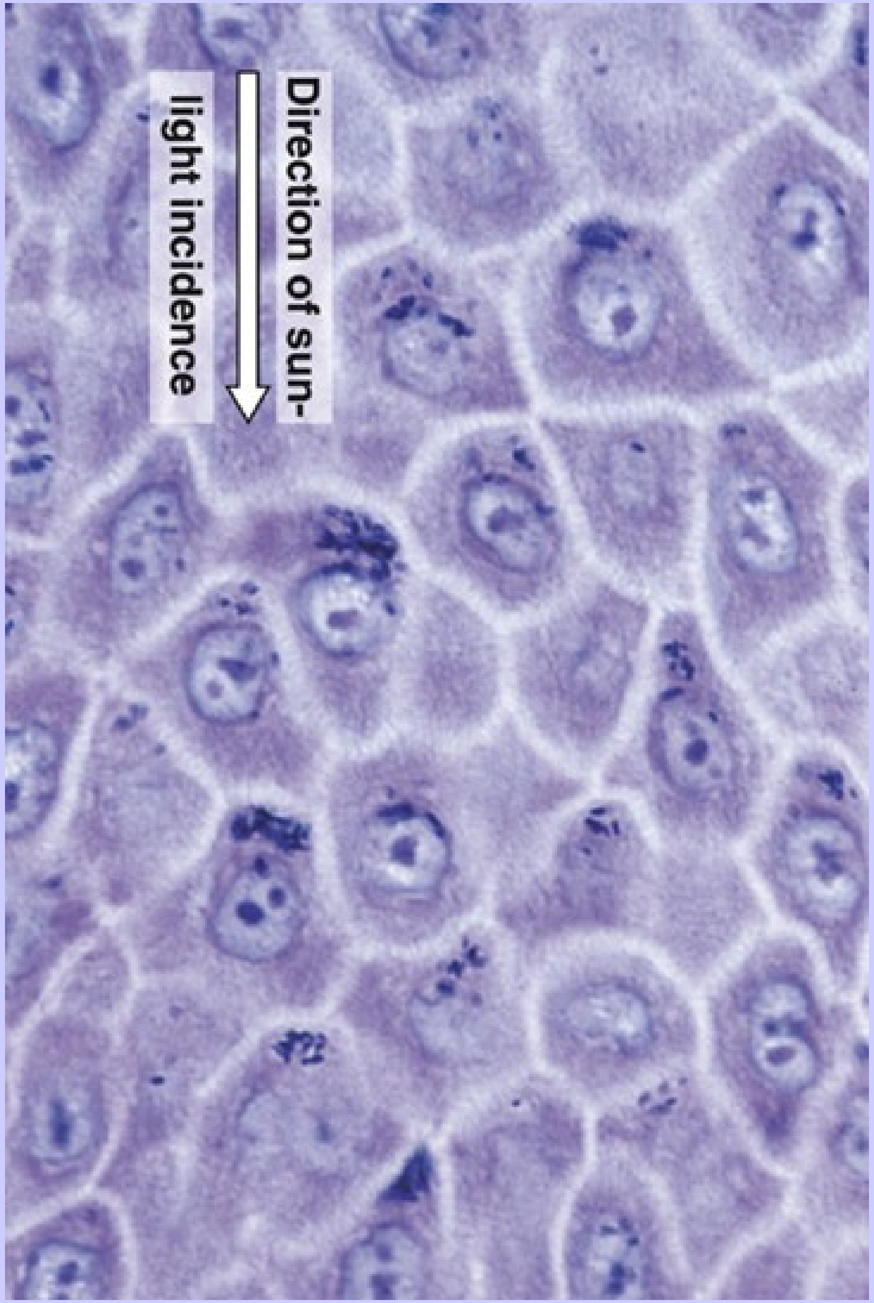


FIGURE 15.9 ▲ Formation of melanin and mechanism of pigment donation. Melanocytes produce lysosome-related membrane-bound structures that originate from the Golgi apparatus as premelanosomes **(1)** that are involved in melanin synthesis. Melanin is produced from tyrosine by a series of enzymatic reactions and its accumulation is visible in the early melanosomes **(2)**. As maturation progresses, melanosomes travel toward the ends of the melanocyte processes. Mature melanosomes **(3)** have a high concentration of melanin and accumulate at the ends of melanocyte processes that invaginate into the keratinocyte's cell membrane **(4)**. Keratinocytes phagocytose the tips of the melanocyte processes containing the melanosomes **(5)**. In the process described as pigment donation, melanin is transferred to neighboring keratinocytes in vesicles containing melanosomes with a small amount of melanocyte cytoplasm **(6)**. Once inside the keratinocytes, melanosomes are released into the cytoplasm **(7)**. Melanosomes are distributed within the keratinocytes with more pronounced accumulation in areas over the nuclei, creating "dark umbrellas" **(8)** that protect the nuclear DNA from the sun's harmful ultraviolet radiation.



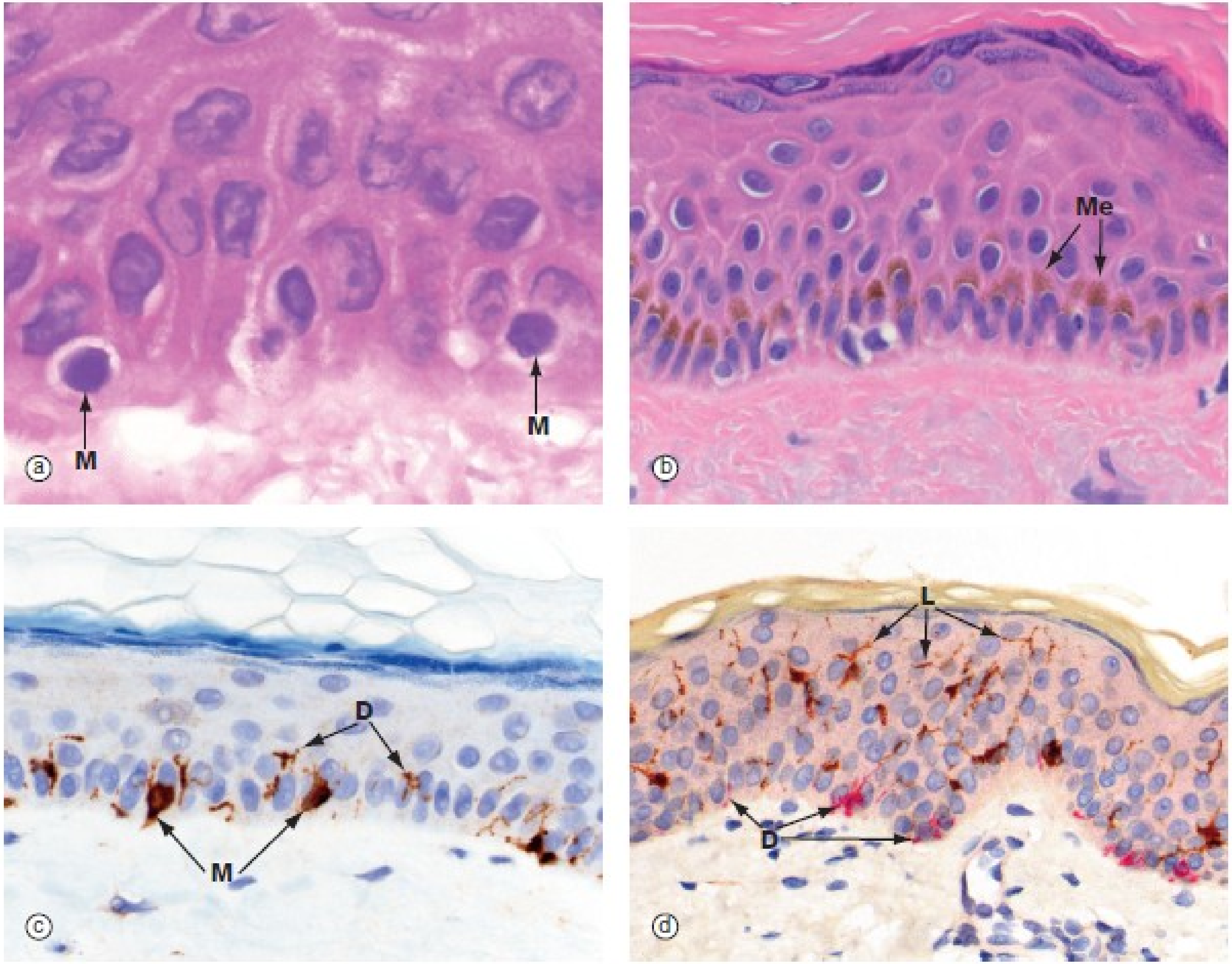


FIG. 9.6 Melanocytes
(a) H&E (HP) (b) H&E, pigmented skin (MP) (c) Immunohistochemistry for melanA (MP) (d) Dual immunohistochemistry for melanA (red) and langerin (brown) (MP)

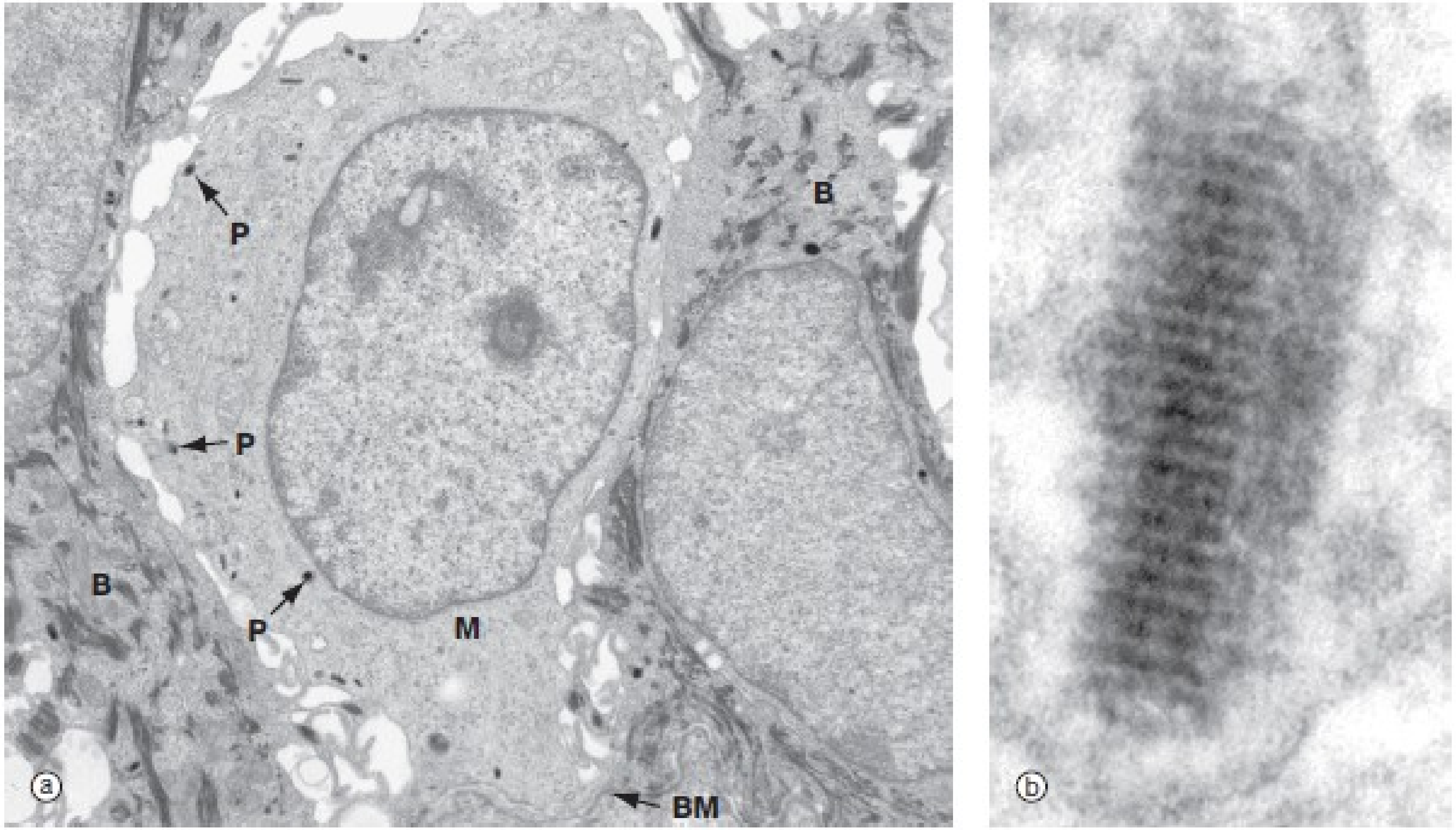


FIG. 9.7 Melanocytes
(a) EM ×15 000 (b) EM ×300 000

At low-power, electron micrograph (a) shows a pale-staining melanocyte **M** between two tonofibril-containing basal keratinocytes **B**; all are sitting on an indistinct basement membrane **BM**. The cytoplasm of the melanocyte has no tonofibrils but contains scanty tiny round or oval dark-staining ***premelanosomes*** and ***melanosomes*** **P** responsible for the synthesis of melanin. Tyrosine is converted into dihydroxyphenylalanine (DOPA) and then polymerised into melanin, which later links to protein to form ***melanoprotein***.

The high magnification, electron micrograph (b) shows the ultrastructural features of a premelanosome. It is a round or cylindrical electron-dense structure with distinct transverse striations and sometimes faint longitudinal striations. Sometimes, an indistinct surrounding membrane can be seen.

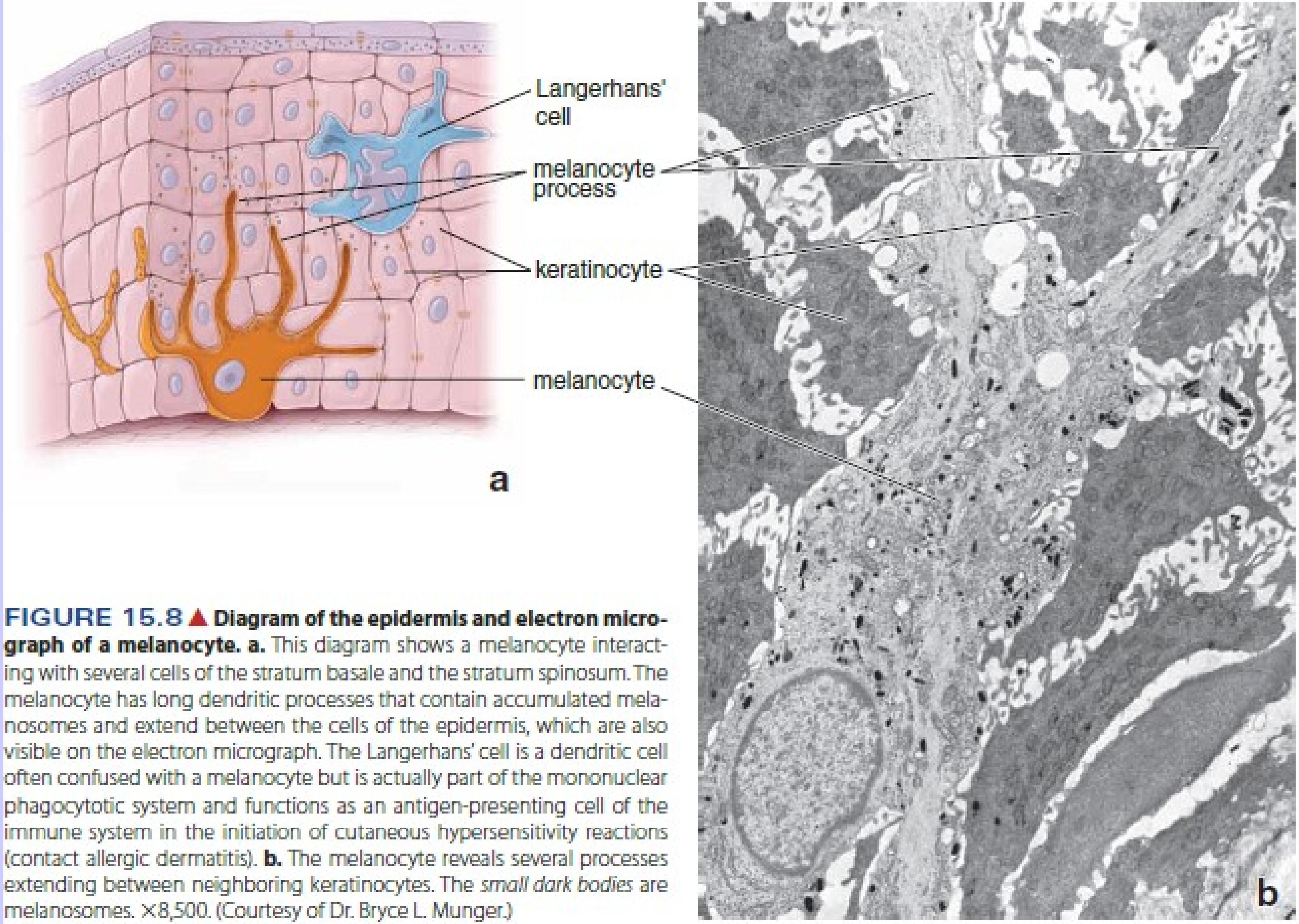


FIGURE 15.8 ▲ Diagram of the epidermis and electron micrograph of a melanocyte. a. This diagram shows a melanocyte interacting with several cells of the stratum basale and the stratum spinosum. The melanocyte has long dendritic processes that contain accumulated melanosomes and extend between the cells of the epidermis, which are also visible on the electron micrograph. The Langerhans' cell is a dendritic cell often confused with a melanocyte but is actually part of the mononuclear phagocytotic system and functions as an antigen-presenting cell of the immune system in the initiation of cutaneous hypersensitivity reactions (contact allergic dermatitis). **b.** The melanocyte reveals several processes extending between neighboring keratinocytes. The *small dark bodies* are melanosomes. ×8,500. (Courtesy of Dr. Bryce L. Munger.)

SKIN

EPIDERMIS

Cell types:

- *Keratinocytes*
- *Melanocytes*
- *Langerhans cells.* Macrophages that function in immunological skin reactions.
- *Merkel's cells*

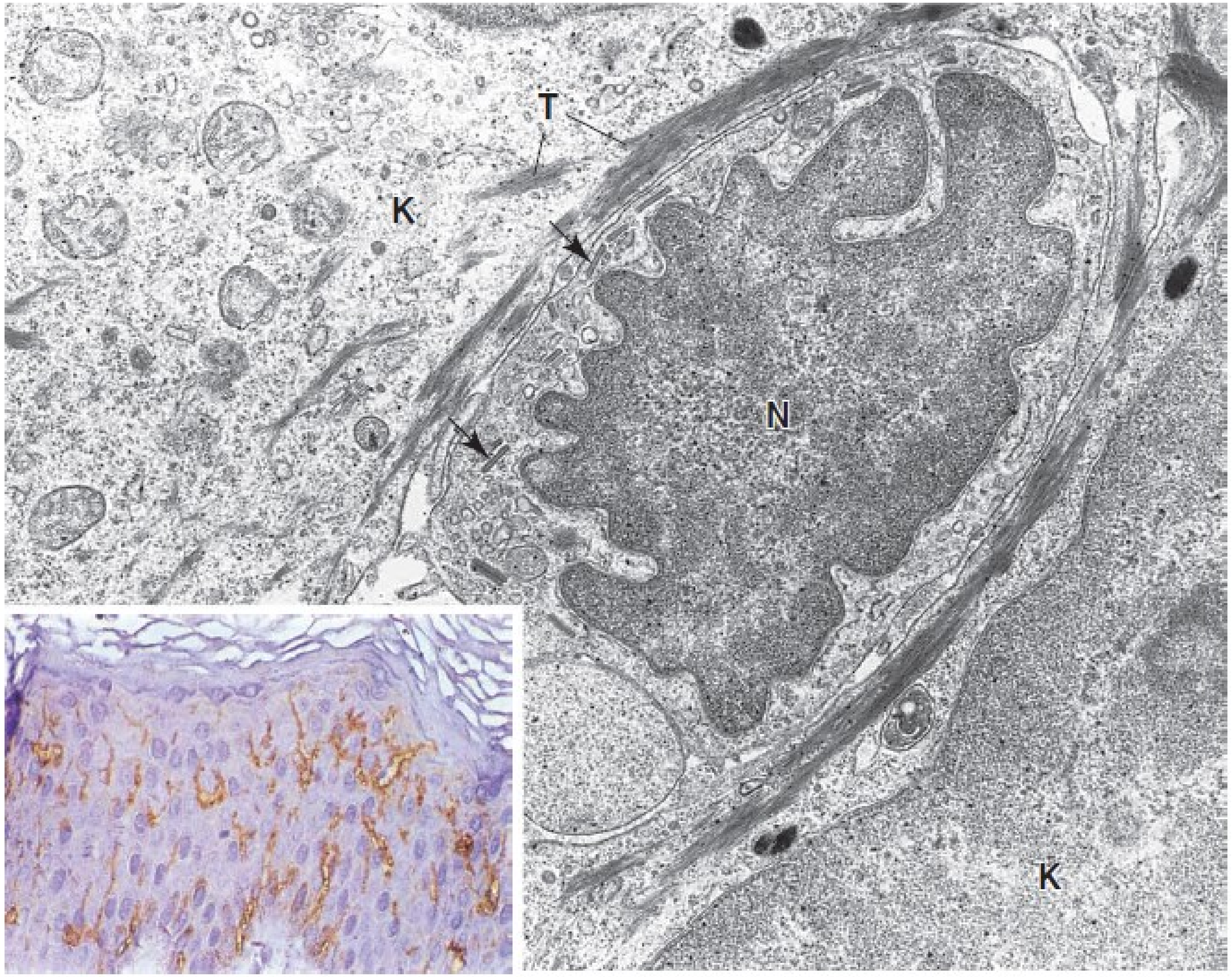
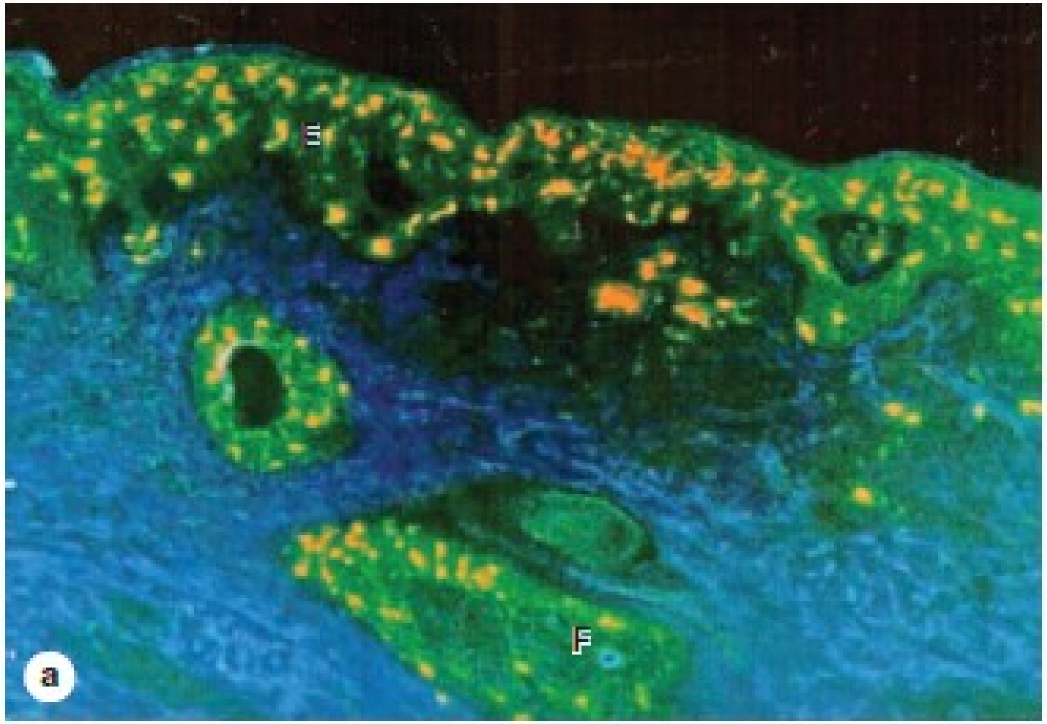
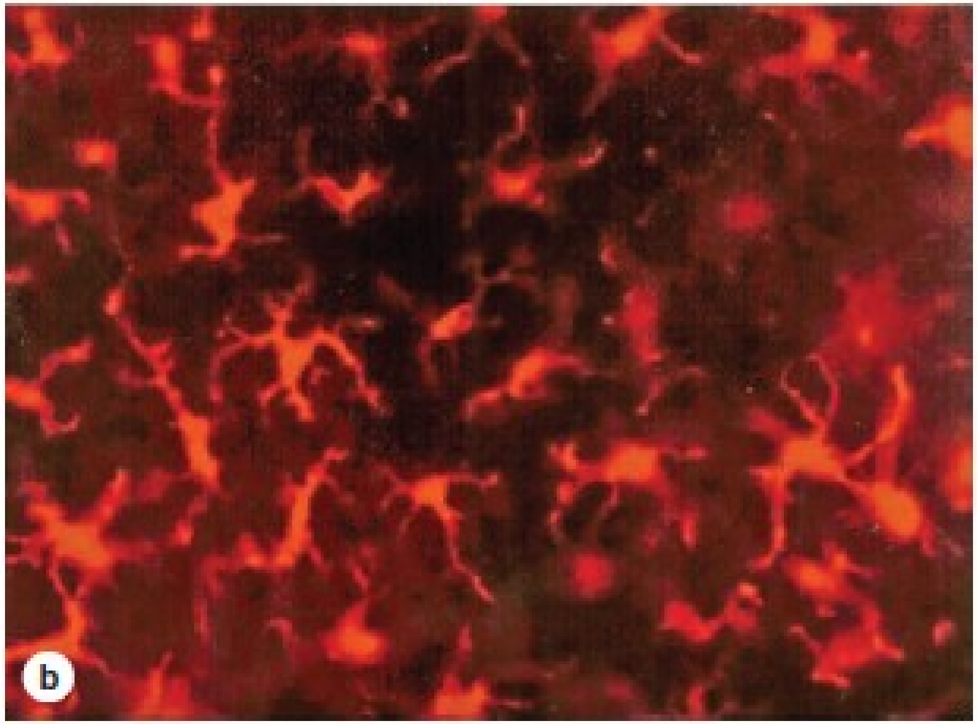


FIGURE 15.10 ▲ Electron micrograph of a Langerhans' cell. The nucleus (*N*) of a Langerhans' cell is characteristically indented in many places, and the cytoplasm contains distinctive rod-shaped bodies (*arrows*). Note the presence of tonofilaments (*T*) in adjacent keratinocytes (*K*) but the absence of these filaments in the Langerhans' cell. ×19,000. **Inset.** Photomicrograph of the epidermis shows the distribution and dendritic nature of the Langerhans' cells that were stained via immunostaining techniques with antibodies against CD1a surface antigen. ×300. (Reprinted with permission from Urmacher CD. Normal Skin. In: Sternberg SS, ed. Histology for Pathologists. Philadelphia: Lippincott-Raven, 1997:25–45.)

FIGURE 18–8 Langerhans cells.





Langerhans cells are dendritic APCs of the epidermis where they comprise an important defense against pathogens and environmental insults. Like other APCs, they develop in the bone marrow, move into the blood circulation, and finally migrate into stratified squamous epithelia where they are difficult to identify in routinely stained sections.

(a) Section of immunostained skin shows Langerhans cells (yellow) abundant in hair follicles (**F**), where many microorganisms live, and throughout the epidermis (**E**). Keratin of the epidermis and follicles is stained green. (X40) Antibodies against langerin/CD207 and keratin.

(b) Face-on view of an epidermal sheet stained using the same antibody showing the network of Langerhans cells among the other epidermal cells, which detects invading microorganisms. After sampling the invaders' antigens, Langerhans cells leave the epidermis and travel to the nearest lymph node to elicit lymphocytes that can mount a collective immune response. (X200; Anti-langerin/CD207)

(*Reproduced, with permission, from Romani N, et al. Acta Path Micro Immunol Scandinavica. 2003;111:725.*)

SKIN

EPIDERMIS

Cell types:

- *Keratinocytes*
- *Melanocytes*
- *Langerhans cells*
- *Merkel's cells*. Touch receptors.

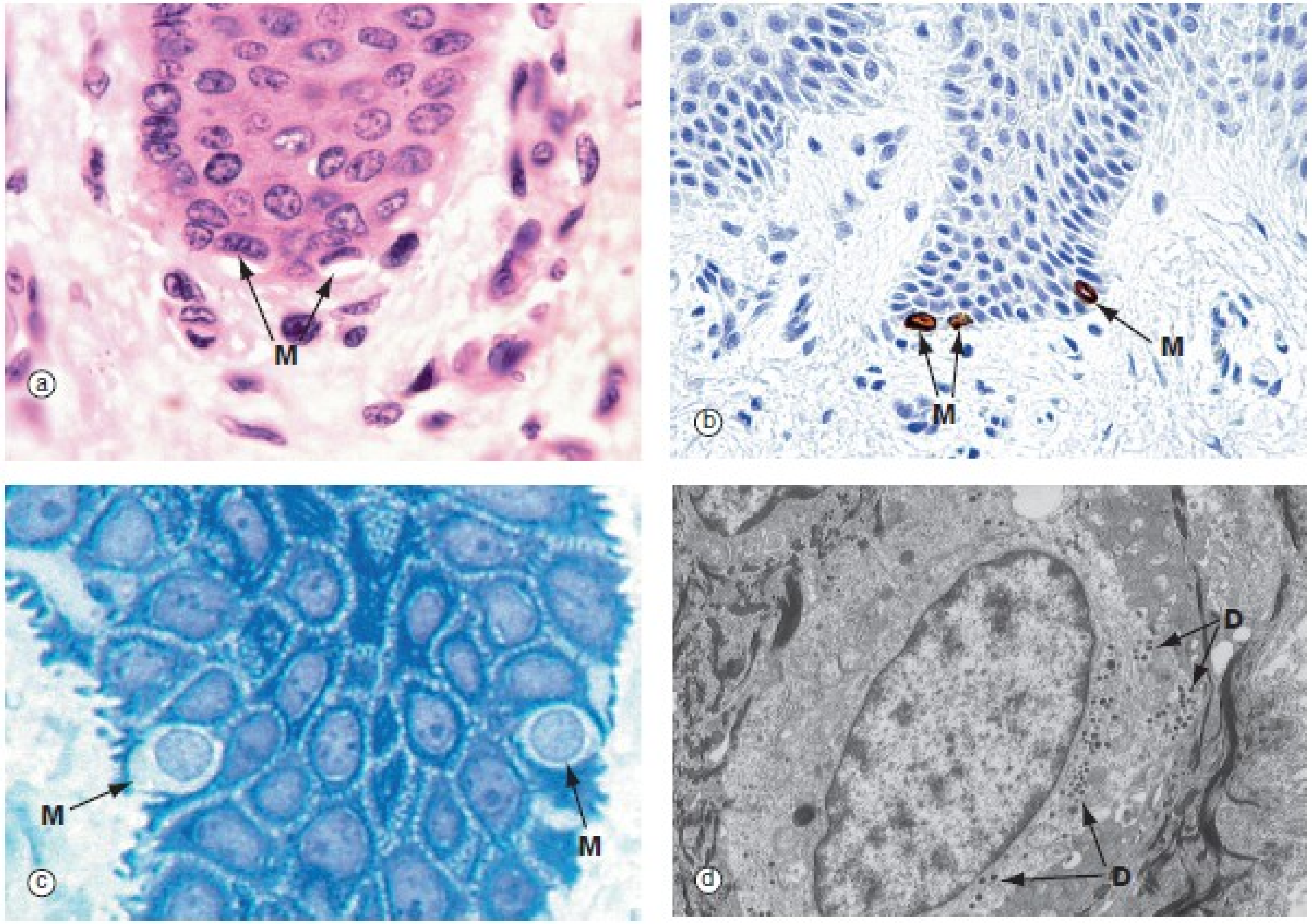
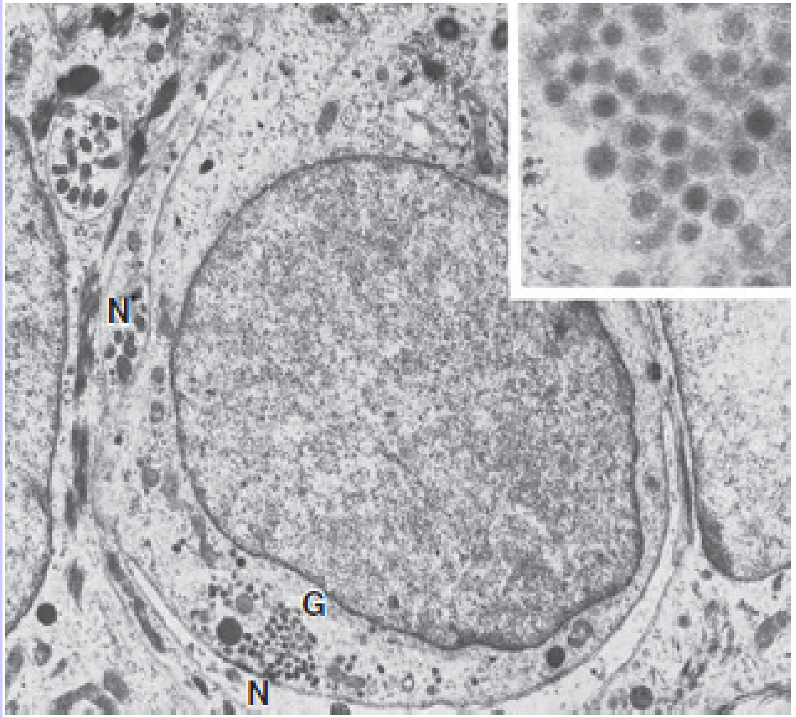


FIG. 9.8 Merkel cell
(a) H&E (MP) (b) Immunohistochemistry for CK20 (MP) (c) Epoxy resin thin section, toluidine blue ×1000 (d) EM ×10 000

Merkel cells are intra-epidermal touch receptors and contain neuroendocrine-type membrane-bound vesicles (dense core granules) in their cytoplasm, particularly near their base where they make synaptic junctions with myelinated sensory nerve twigs in the upper dermis. They are difficult to detect in routine H&E sections.

Micrograph (a) shows two Merkel cells M in the basal layer of epidermis. They are rounded cells with pale-staining cytoplasm. The immunohistochemical preparation in micrograph (b) illustrates three Merkel cells M. Micrograph (c) shows Merkel cells with pale nuclei and cytoplasm, while in electron micrograph (d) the dense core granules D can be seen.

FIGURE **18–9** **Merkel or tactile cell.**



Merkel cells in the epidermis' basal layer are modified keratinocytes that function as highly sensitive mechanoreceptors, especially abundant in skin of the fingertips and external genitalia. This TEM of a Merkel cell shows a mass of Golgi-derived dense-core cytoplasmic granules (**G**) near the basolateral cell membrane, which is in direct synaptic contact with the expanded, disc-like ending of an unmyelinated sensory nerve fiber (**N**) that has penetrated the epidermis. (X14,000) Inset: Granules are similar in morphology and content to the granules of many neuroendocrine cells. (X61,500) Here the vesicles contain both classic neurotransmitters like serotonin and a variety of neuropeptides. Exocytosis of these agents occurs when slight mechanical displacement of the epidermis activates calcium-channels in the Merkel cell membrane, initiating a neural impulse producing the sensation of touch.

FIGURE 15.11 ▲ Electron micrograph of a Merkel's cell. The cell has small neurosecretory granules in the cytoplasm and makes contact with a peripheral nerve terminal (*NT*) of a sensory neuron. The dermis (*D*) is in the *lower part* of the micrograph. ×14,450. (Courtesy of Dr. Bryce L. Munger.)

SKIN

DERMIS

Composition:

- *Papillary layer*

1. Located immediately beneath the basement membrane of the epidermis, forming the dermal papillae
2. Thin layer composed of loose connective tissue
3. Contains small blood vessels, nerves, lymphatics, and the sensory receptors, Meissner's corpuscles

- *Reticular layer*
    - Located between the papillary layer and the hypodermis
    - Thick layer composed of dense, irregular connective tissue
    - Contains larger nerves and blood vessels, glands, hair follicles, and the sensory receptors, Pacinian corpuscles and Ruffini end organs

Vasculature of the dermis:

- Papillary plexus located in the dermal papillae
- Cutaneous plexus located in the reticular layer of the dermis
- Arteriovenous anastomoses allow shunting of blood between papillary and cutaneous plexuses for temperature regulation.

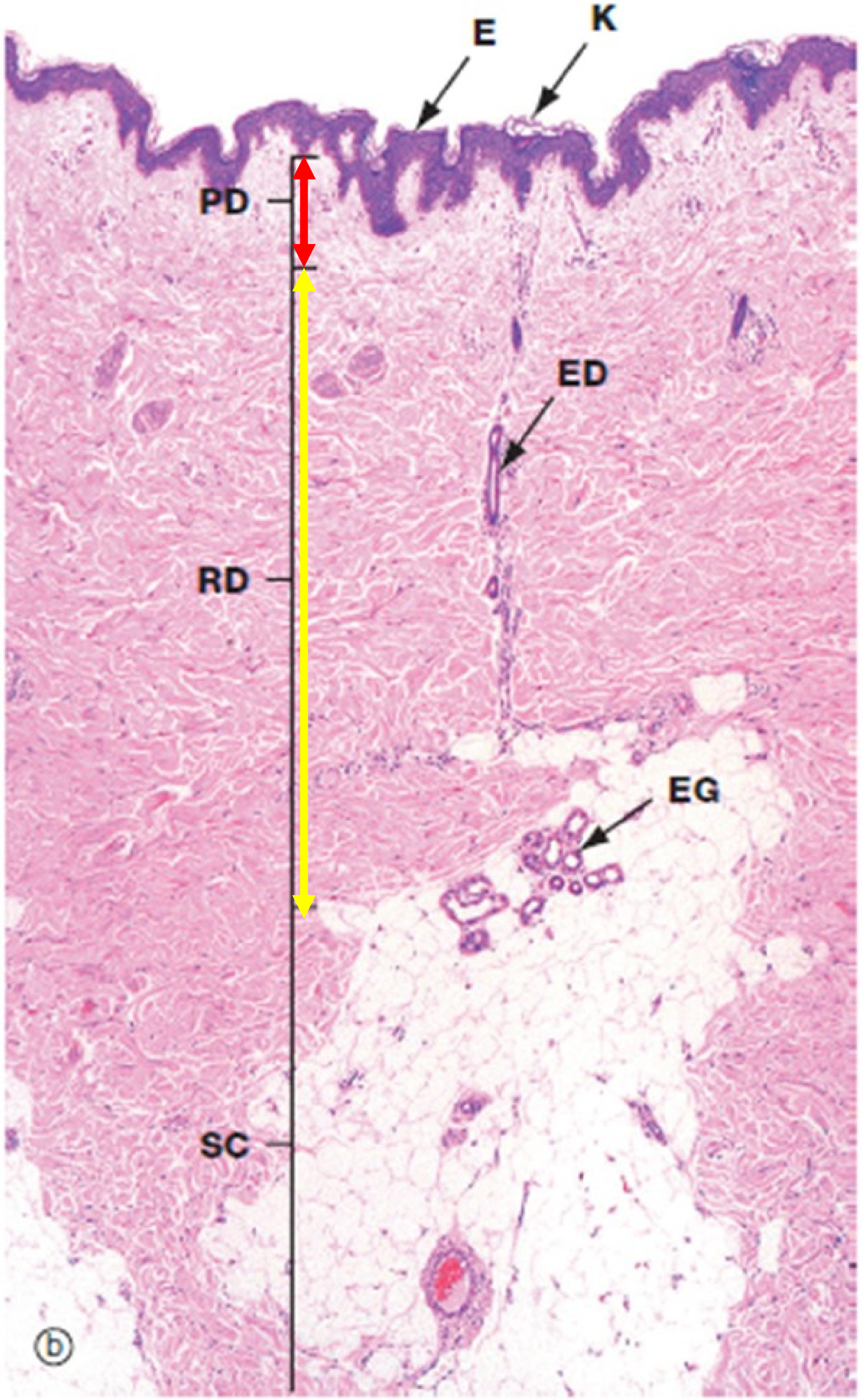


FIG. 9.1 Skin architecture
(a) Diagram (b) H&E (LP)

These illustrations show the basic structure of the skin, with the three component layers: ***epidermis, dermis*** and ***subcutis***.

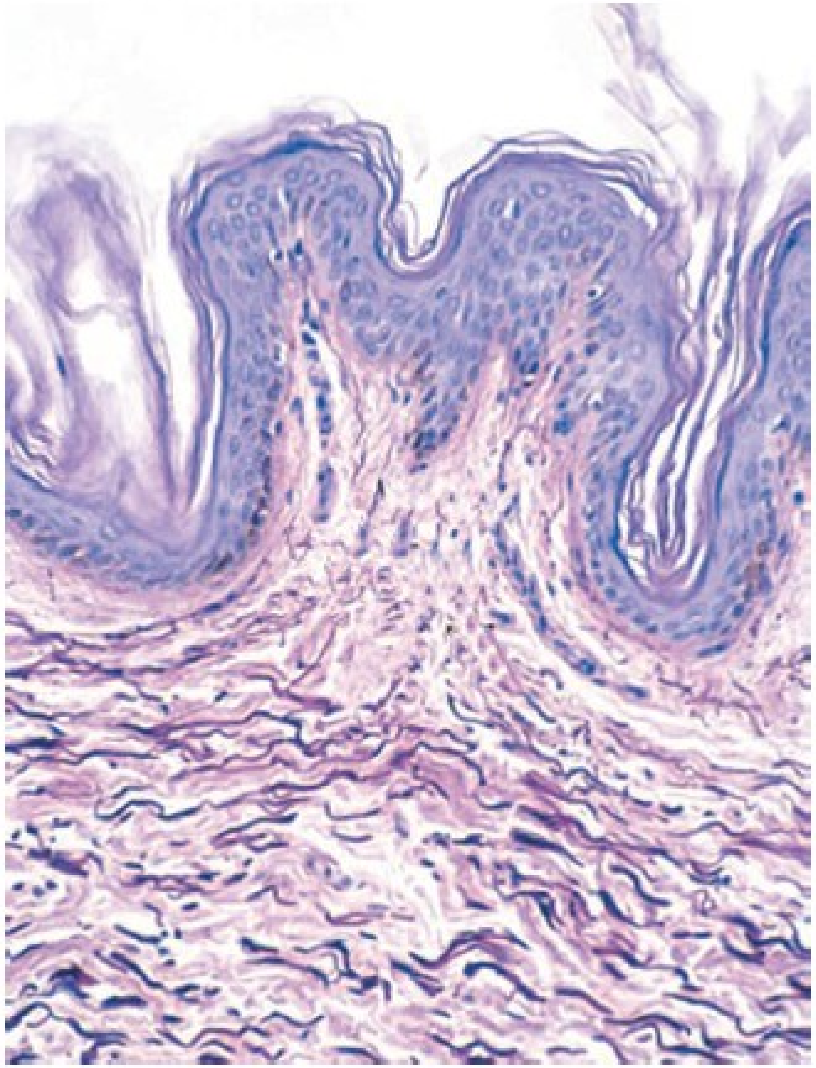
The surface layer in contact with the exterior is the epidermis **E**, a highly specialised self-regenerating stratified squamous epithelium which produces a non-living surface rich in a protein, ***keratin*** **K**, that is tough and protective and is also partially water resistant (see Ch. 5). The epidermis also contains non-epithelial cells: ***melanocytes*** produce melanin pigment to protect against UV light, ***Langerhans cells*** act as antigen-presenting cells and induce immune responses to new antigens and ***Merkel cells*** act as touch receptors. The epidermis is tightly bound to the underlying dermis by a specialised basement membrane. Additional resistance to frictional shearing force is provided by a series of epidermal downgrowths (***rete ridges***) which extend into the superficial dermis, with their papillary dermal mirror images projecting upwards (***dermal papillae***) to provide stronger tethering. These are most developed where exposure to shearing forces is almost constant (e.g. sole, palm).

The dermis immediately adjacent to the epidermis is called the ***papillary dermis*** **PD**; it has relatively fine collagen fibres and contains numerous small blood vessels, sensory nerve endings and sensory structures. The ***reticular dermis*** **RD** is the deeper tough layer of horizontally arranged collagen and elastin fibres with fibroblasts.

The deepest layer is the subcutis **SC**, also called the ***panniculus*** or ***hypodermis***. It is a layer of adipose tissue often compartmentalised by fibrous septa, extending downwards from dermis to the underlying structural connective tissue fascia. The subcutis acts as a shock absorber and thermal insulator as well as a fat store.

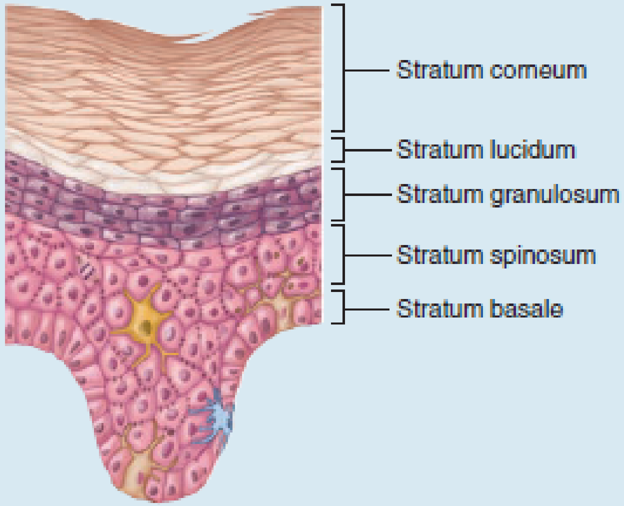
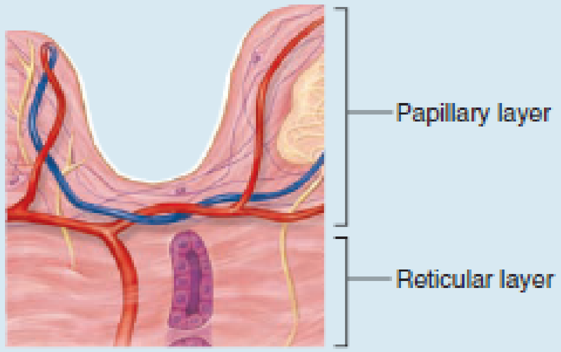
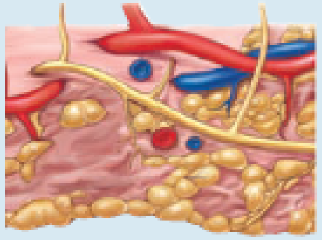
The dermis and subcutis contain an assortment of skin ***adnexa (appendages)*** such as ***hair follicles, sebaceous glands, eccrine (sweat) glands*** **EG** and ducts **ED** and, in some areas, ***apocrine glands***.

FIGURE **18–10** **Elastic fibers of dermis.**



A section of thin skin stained for elastic fibers shows the extensive distribution of these darkly stained fibers among the eosinophilic collagen bundles. In the dermal papillary layer, the diameter of fibers decreases as they approach the epidermis and insert into the basement membrane. (X100; Weigert elastic stain)

TABLE 18–1 Summary of skin and subcutaneous layers.

Layer	Specific Layer	Description
Epidermis 	Stratum corneum	Most superficial layer; 20-30 layers of dead, flattened, anucleate, keratin-filled keratinocytes; protects against friction and water loss
	Stratum lucidum	2-3 layers of anucleate, dead cells; seen only in thick skin
	Stratum granulosum	3-5 layers of keratinocytes with distinct kerato-hyaline granules
	Stratum spinosum	Several layers of keratinocytes all joined by desmosomes; Langerhans cells present
	Stratum basale	Deepest, single layer of cuboidal to low columnar cells in contact with basement membrane; mitosis occurs here; melanocytes and Merkel cells also
Dermis 	Papillary layer	More superficial layer of dermis; composed of areolar connective tissue; forms dermal papillae; contains subpapillary vascular plexus
	Reticular layer	Deeper layer of dermis; dense irregular connective tissue surrounding hair follicles, sebaceous glands and sweat glands, nerves, and deep plexus of blood vessels extending into subcutaneous layer
Subcutaneous layer 	No specific layers	Not considered part of the integument; deep to dermis; composed of areolar and adipose connective tissue

SKIN

STRUCTURES ASSOCIATED WITH THE SKIN

- **Sensory structures**
  - Nonencapsulated. Free nerve endings in the epidermis, responsive to touch, pressure, heat, cold, and pain
  - Encapsulated pressure receptors
    - *Meissner's corpuscle*
      - Located at the apex of a dermal papilla
      - Consists of a coil of Schwann cells around a nerve terminal
      - Responds to light touch
    - *Pacinian corpuscle*
      - Located in the dermis and hypodermis
      - Consists of concentric layers of endoneurial cells around a nerve terminal
      - Responds to vibration and deep pressure
    - *Ruffini ending*
      - Located in the dermis
      - Consists of groups of nerve terminals surrounded by a thin connective tissue capsule
      - Responds to touch and pressure

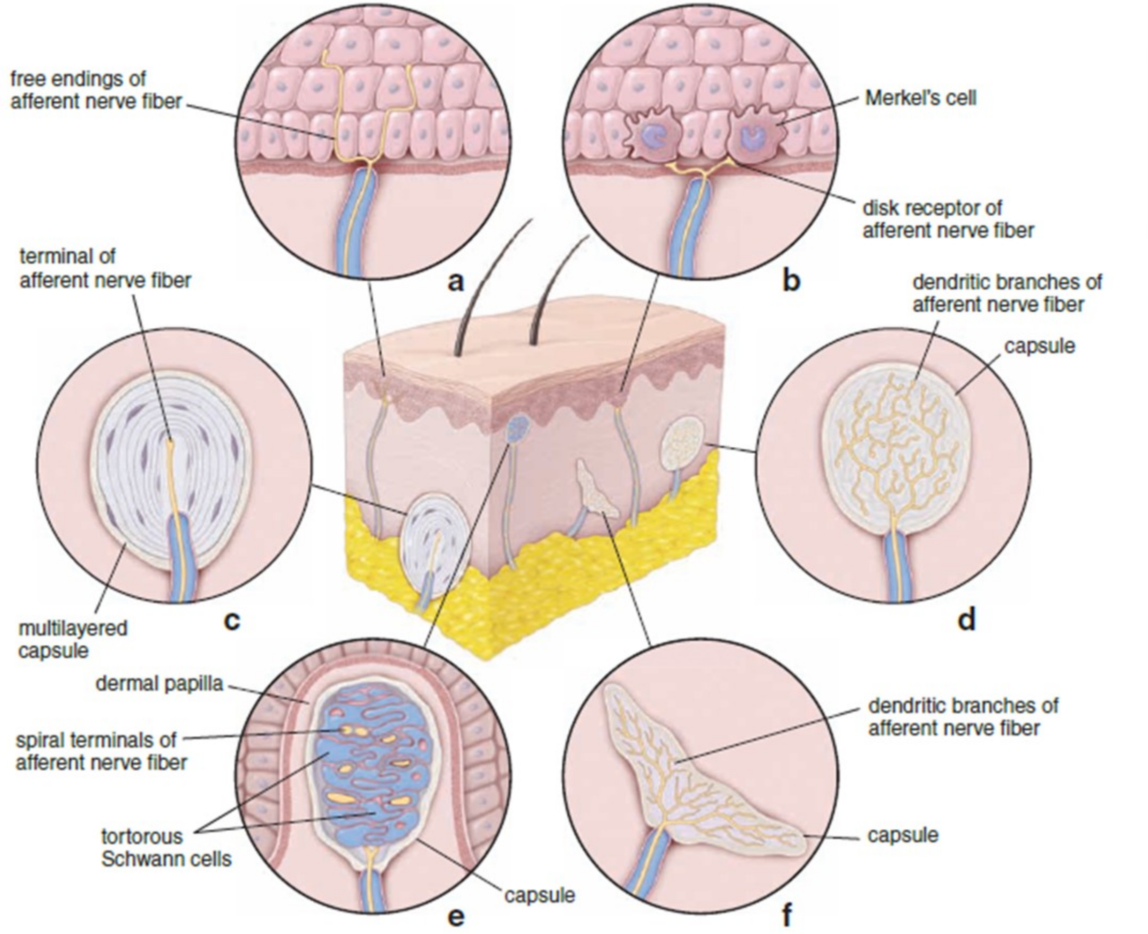
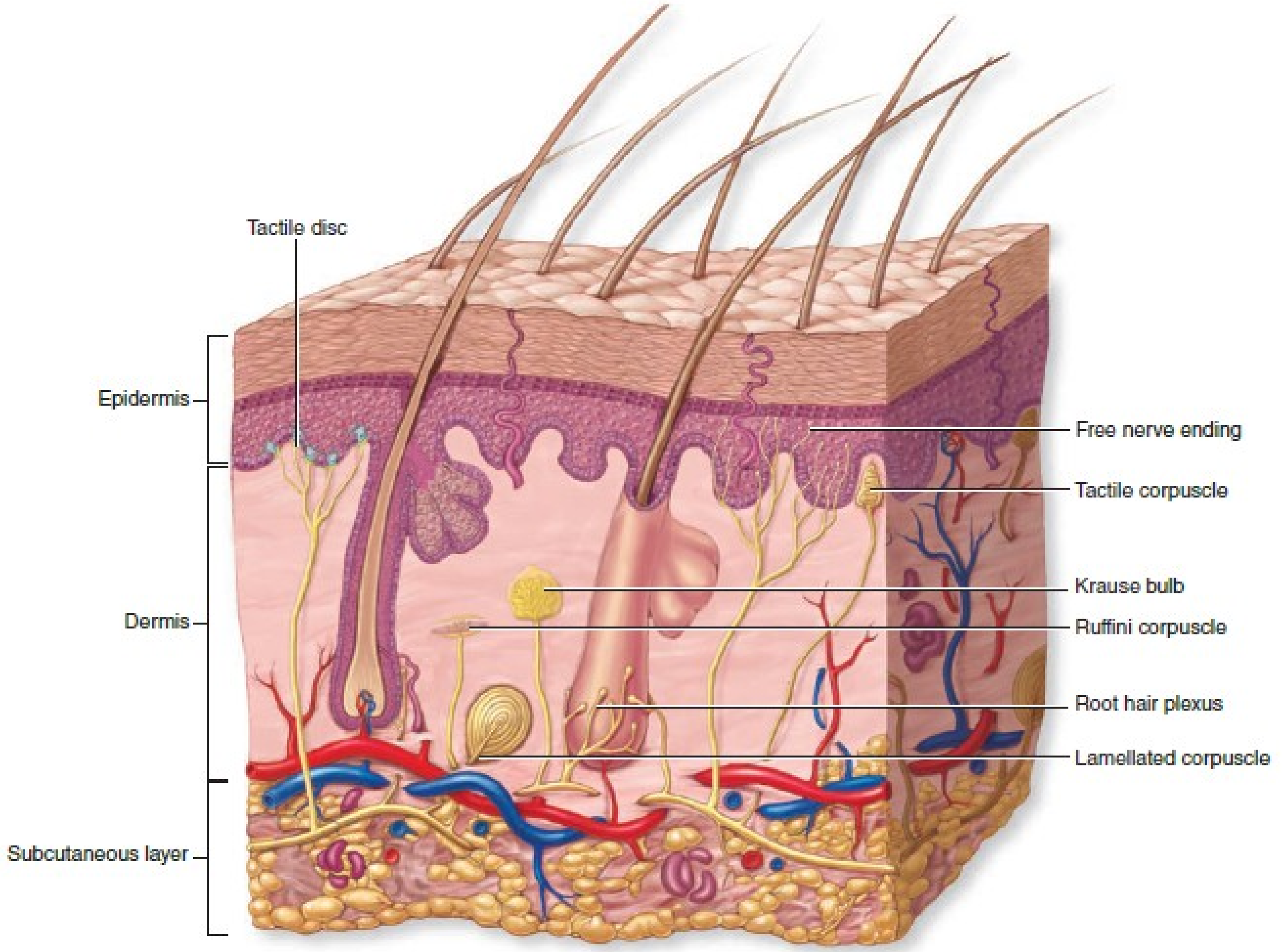


FIGURE 15.12 ▲ Diagram of the sensory receptors in skin. a. Epidermal free endings. **b.** Merkel's corpuscles containing Merkel's cells and disc receptors of afferent myelinated nerve fiber. **c.** Pacinian corpuscle located in the deep layer of deep dermis and hypodermis. **d.** Krause's end bulb serves as cold receptor. **e.** Meissner's corpuscle in dermal papilla. **f.** Ruffini's corpuscle in deep layers of the dermis. Note that sensory nerve fibers in receptors **c–f** are encapsulated.

FIGURE **18–11** **Tactile receptors.**



Skin contains several types of **sensory receptors**, with or without capsules of collagen and modified Schwann cells. Most are difficult to see in routine preparations. In the epidermis are **free nerve endings** and tactile discs of nerve fibers associated with **Merkel cells** in the basal layer. Both have unencapsulated nerve fibers, as does the **root hair plexus** around the bases of hair follicles in the dermis. They detect light touch or movement of hair, although epidermal free nerve endings also detect pain and temperature extremes.

More complex, encapsulated tactile receptors are located in the dermis and hypodermis, and include **Meissner corpuscles** for light touch, **lamellated (pacinian) corpuscles** detecting pressure and high-frequency vibration, **Krause end bulbs** for detection of low-frequency vibrations/movements, and **Ruffini corpuscles** detecting tissue distortion. The latter two receptors are less widely distributed in skin and less commonly seen.

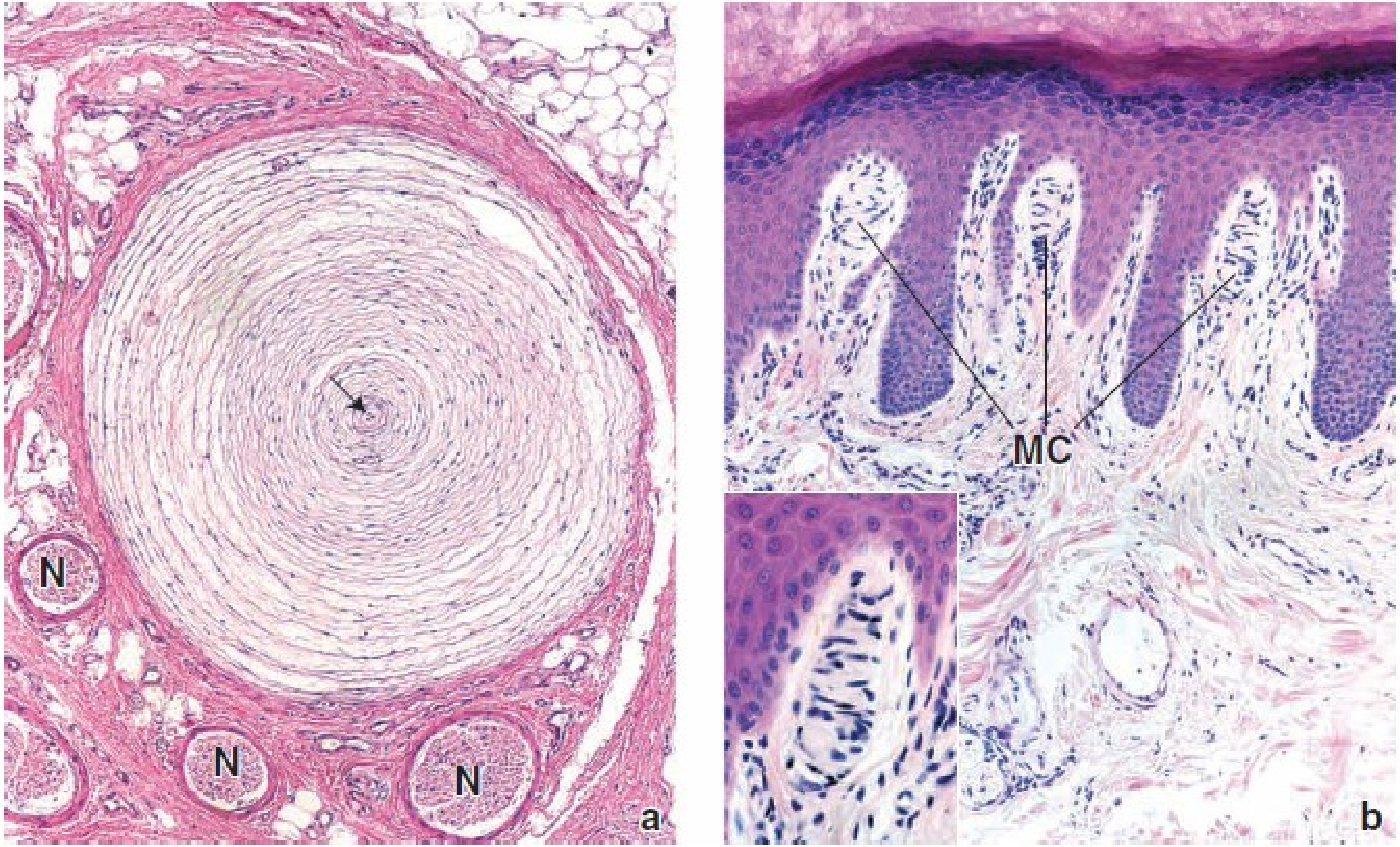
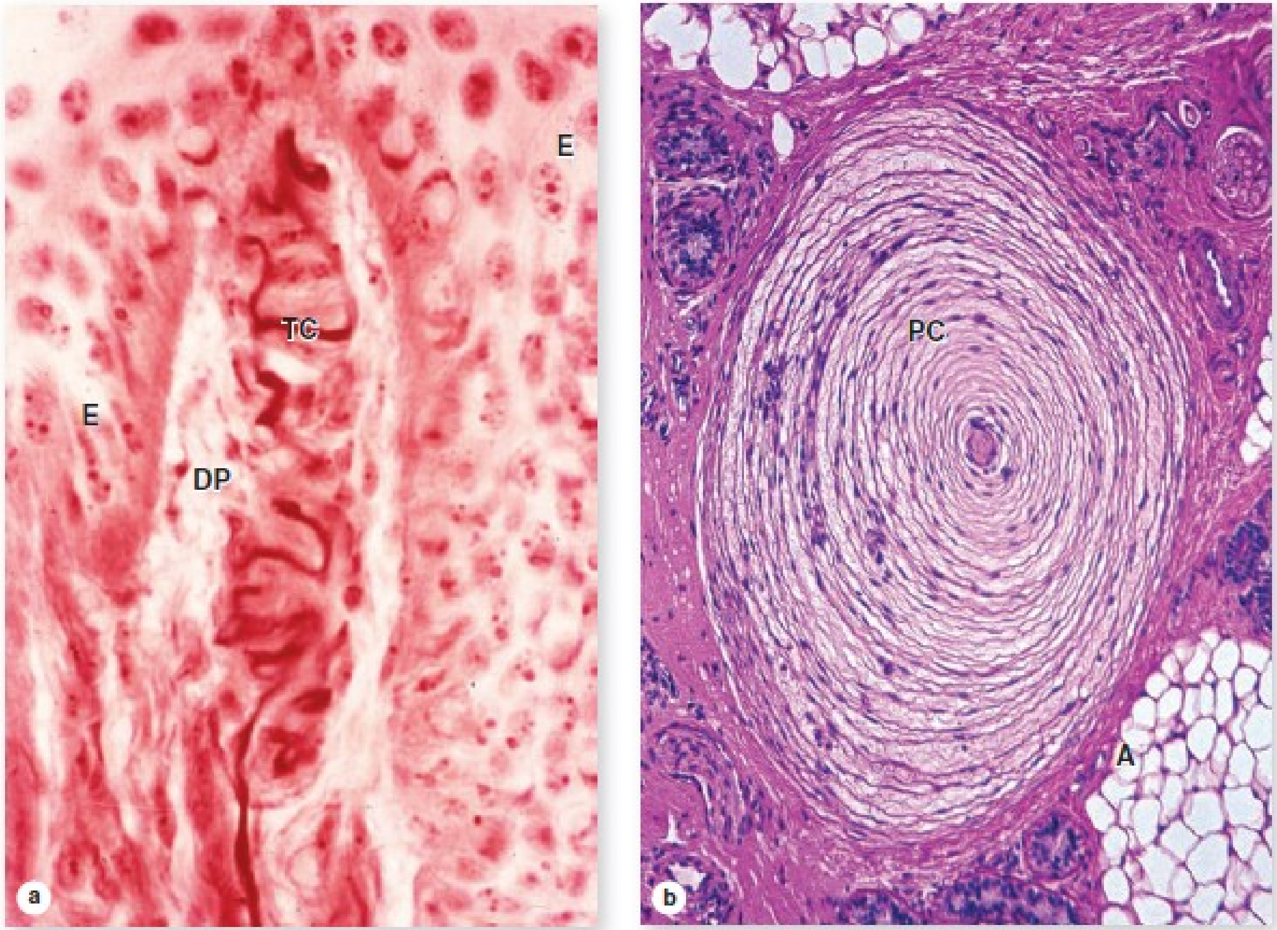


FIGURE 15.13 ▲ Pacinian and Meissner's corpuscles in H&E preparations. a. In this photomicrograph, the concentric cellular lamellae of the Pacinian corpuscle are visible because of flat, fibroblast-like supportive cells. Although not evident within the tissue section, these cells are continuous with the endoneurium of the nerve fiber. The spaces between lamellae contain mostly fluid. The neural portion of the Pacinian corpuscle travels longitudinally through the center of the structure (*arrow*). Several nerves (*N*) are present adjacent to the corpuscle. ×85. **b.** Three Meissner's corpuscles (*MC*) are shown residing within the dermal papillae. Note the direct proximity of the corpuscle to the undersurface of the epidermis. ×150. **Inset.** A higher magnification of a Meissner's corpuscle. The nerve fiber terminates at the superficial pole of the corpuscle. Note that supporting cells are oriented approximately at right angles to the long axis of the corpuscle. ×320.

FIGURE **18–12** **Meissner and lamellated (pacinian) corpuscles.**



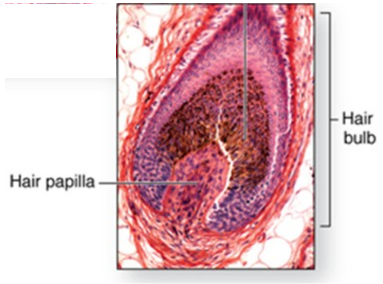
Micrographs show the two most commonly seen sensory receptors of skin.

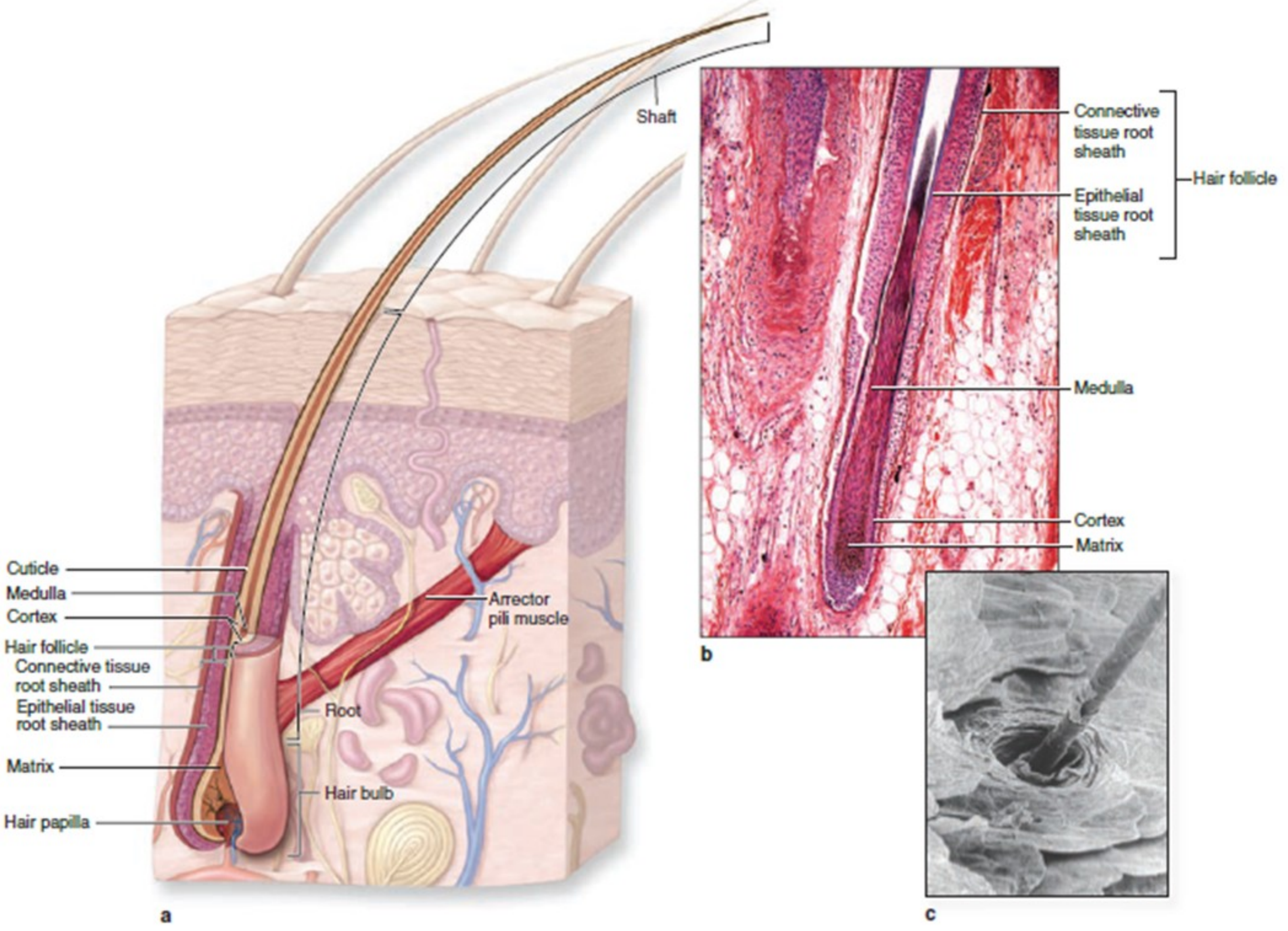
(a) Meissner tactile corpuscles (**TC**) are specialized to detect light touch and are frequently located in dermal papillae (**DP**), partially surrounded by epidermis (**E**). They are elliptical, approximately 150-µm long, with an outer capsule (from the perineurium) and thin, stacked inner layers of modified Schwann cells, around which course nerve fibers. (X400; H&E)

(b) Lamellated (pacinian) corpuscles (**PC**) detect coarse touch or pressure and are large oval structures, frequently 1 mm in length, found among adipose tissue (**A**) deep in the reticular dermis or in the subcutaneous tissue. Here the outer connective tissue capsule surrounds 15-50 thin, concentric layers of modified Schwann cells, each separated by slightly viscous interstitial fluid. Several axons enter one end of the corpuscle and lie in the cylindrical, inner core of the structure. Movement or pressure of this corpuscle from any direction displaces the inner core, leading to a nerve impulse. (X40; H&E)

STRUCTURES ASSOCIATED WITH THE SKIN

- **Hair follicles**
  - *Hairs* are elongated keratinized structures derived from invaginations of the epidermis (hair follicules)
  - Consist of a *bulb* at the base of the follicle that is located in the hypodermis or in the deep layers of the dermis. *Internal and external sheaths* surround the growing hair shaft as it passes though the dermis and epidermis.
  - An *arrector pili muscle* attaches a hair follicle to the papillary layer of the dermis. Contraction provides elevation of the hair, forming "goose-bumps."





All types of body hair have a similar composition and form in hair follicles derived from the epidermis but extending deep into the dermis.

(a) The diagram shows major parts of a hair and its follicle, including vascularized, nutritive hair dermal **papilla** and the **arrector pili muscle** that pulls the hair erect.

(b) A longitudinal section of a hair root and bulb shows the **matrix**, **medulla,** and **cortex** in the root and the surrounding **epithelial and connective tissue** sheaths. Cells of the hair bulb matrix proliferate, take up melanin granules, and undergo keratinization to differentiate as the three concentric layers of the hair. (X70; H&E)

(c) The outermost layer of the hair is the thin **cuticle**, composed of shingle-like cells, shown in this SEM of a hair shaft emerging at the stratum corneum. (X260)

SKIN

STRUCTURES ASSOCIATED WITH THE SKIN

- *Anagen* – growth periods
- *Catagen* – regression of follicle
- *Telogen* – inaktivity

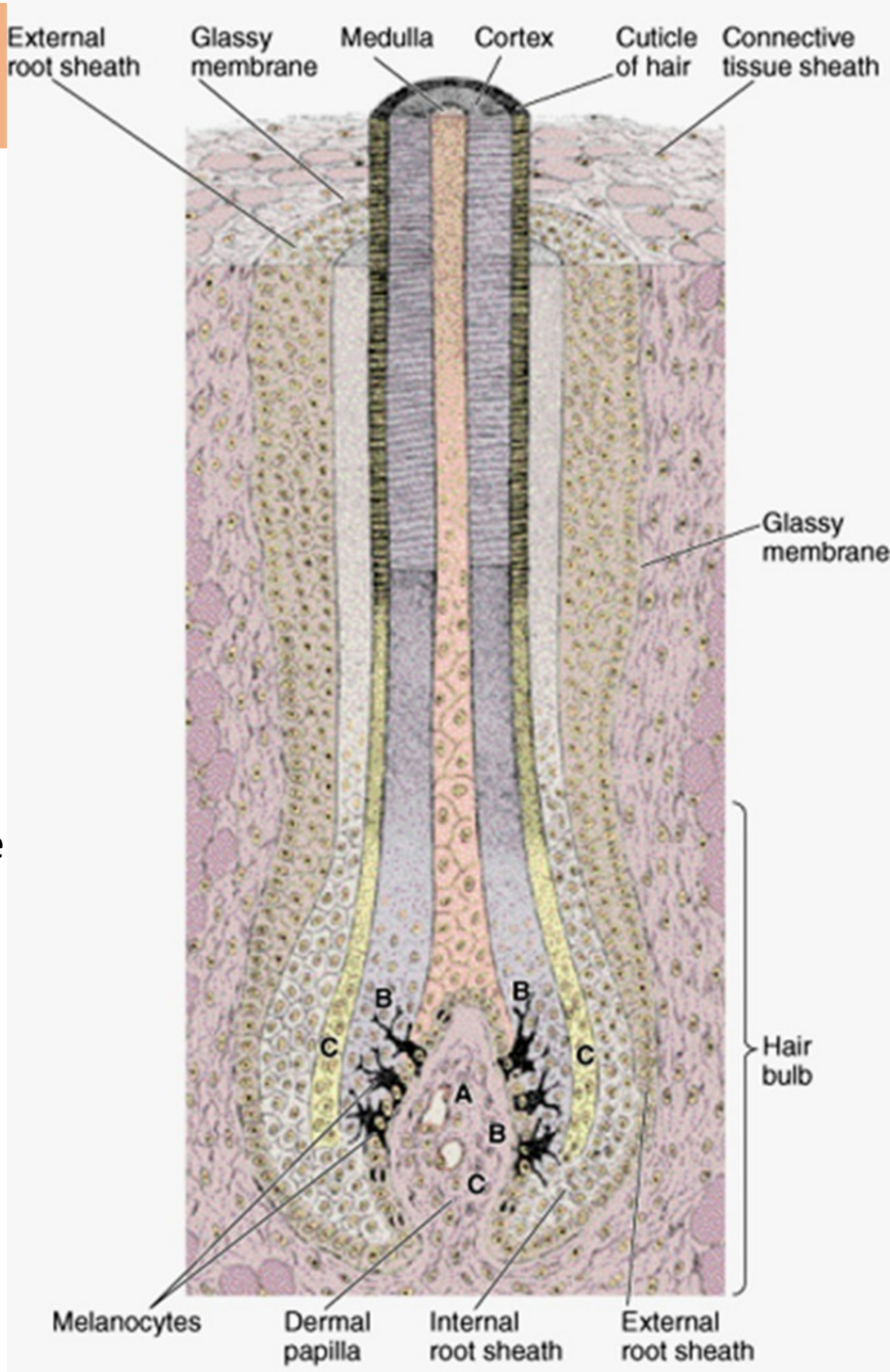
- Hair follicle
- Epithelial tissue root sheath
- Connective tissue root sheath

- Shaft (beyond epidermis)
- Root
- Hair bulb (terminal dilatation)
- Dermal papila (with capillary network)

- Melanocytes
  - in the hair bulb
  - among the keratinocytes
  - transfer melanin granules into the epithelial cells

- Glassy membrane
  - Separating the hair follicle from the dermis
  - An acellular hyaline layer, the thickened basement membrane

- Papila is covered by cells that form the hair root and develop into the hair shaft.
- A – the central cells produce large, vacuolated, moderately keratinized cells that form the **medulla** of the hair
- B - laterally located cells, produce the **cortex** of the hair
- C – cells forming hair **cuticle**
- Peripheral epithelial cells develop into the internal and external root sheaths.
- The external root sheath is continuous with the epidermis
- The cells of the internal root sheath disappear at the level of the opinings of the sebaceous gland ducts.



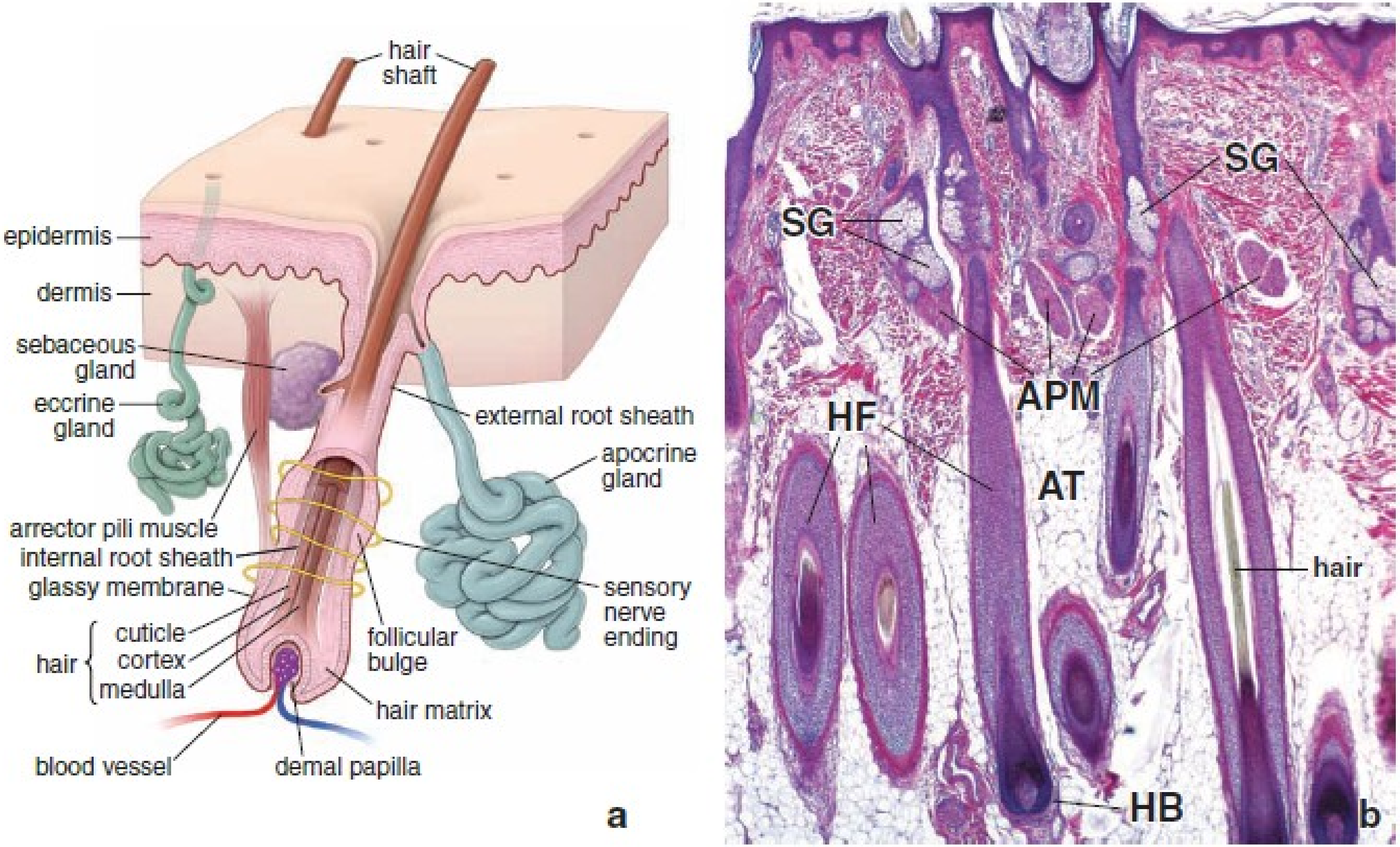
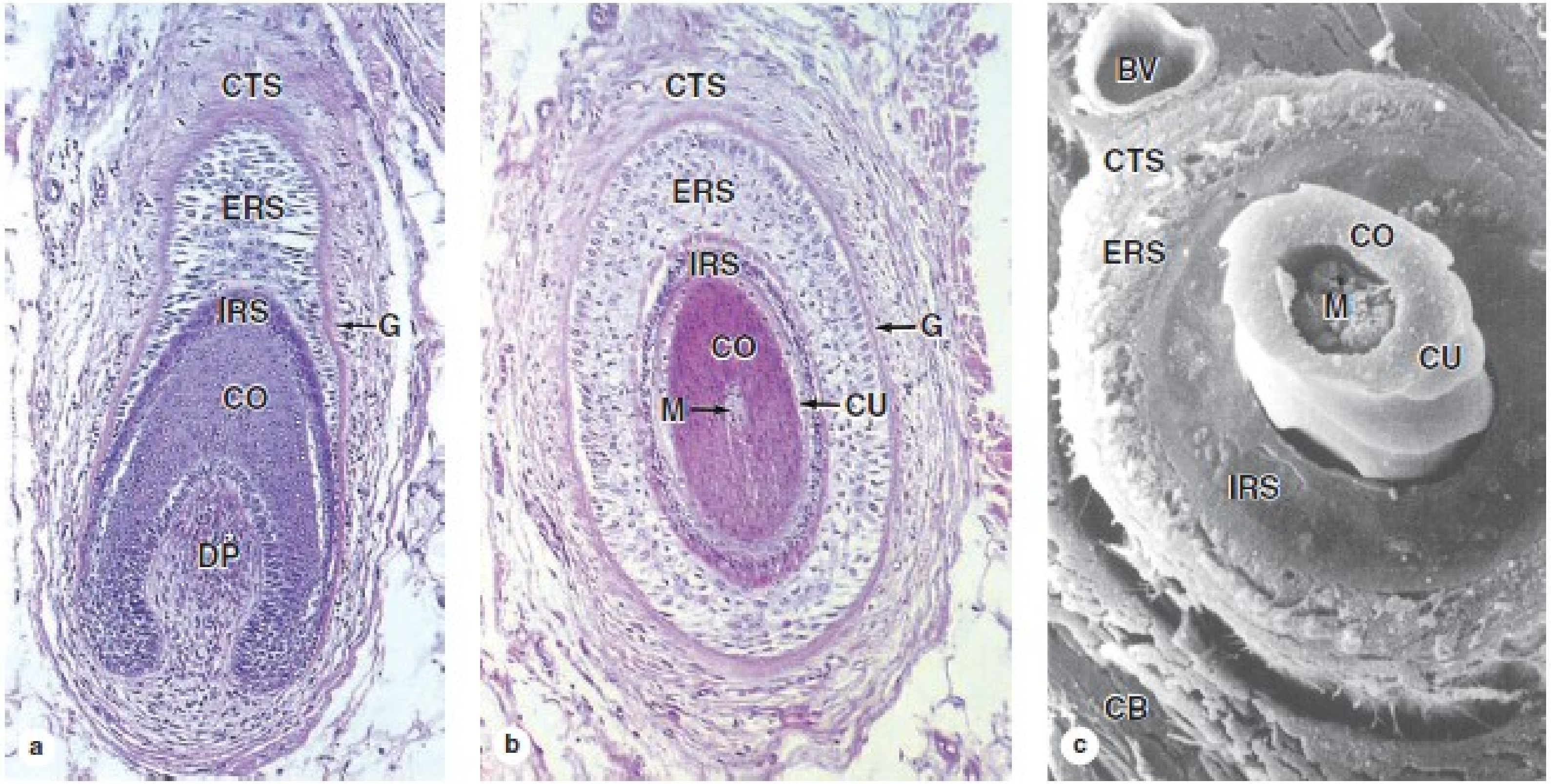


FIGURE 15.14 ▲ Hair follicle and other skin appendages. a. Diagram showing a hair follicle. Note the cell layers that form the hair shaft and the surrounding external and internal root sheaths. The sebaceous gland consists of the secretory portion and a short duct that empties into the infundibulum, the upper part of the hair follicle. The arrector pili muscle accompanies the sebaceous gland; contraction of this smooth muscle assists in gland secretion and discharges the sebum into the infundibulum of the hair follicle. Projection of the external root sheath near insertion of the arrector pili muscle forms the follicular bulge that contains epidermal stem cells. Nerve endings (*yellow*) surround the follicular bulge with nearby insertion of arrector pili muscle. The apocrine sweat gland also empties into the infundibulum. Note that eccrine sweat glands are independent structures and are not associated directly with the hair follicle. **b.** Photomicrograph of H&E–stained section of thin skin from human scalp. The growing end of a hair follicle consists of an expanded hair bulb (*HB*) of epithelial cells that is invaginated by a connective tissue dermal papilla. Hair matrix that fills the bulb consists of cells that differentiate into the hair shaft and the internal root sheath of the hair follicle (*HF*). Note that several oblique and longitudinal sections of the hair follicles are embedded in the adipose tissue (*AT*) of the hypodermis. Some of them reveal a section of the hair. Sebaceous glands (*SG*) are visible in conjunction with the infundibulum of the hair follicle. ×60. APM, arrector pili muscle.

FIGURE 18–14 Layers of a hair and its follicle.



(a) The base of a hair follicle sectioned obliquely shows the vascularized dermal papilla (**DP**) continuous with the surrounding connective tissue sheath (**CTS**). The papilla is enclosed by the deepest part of the epithelial sheath, which is continuous with both the internal root sheath (**IRS**) and external root sheath (**ERS**). Both of these layers are in turn continuous with the stratified epidermis. Just outside the ERS is the glassy membrane (**G**) that is continuous with the basement membrane of the epidermis. The epithelial cells (keratinocytes) around the papilla proliferate and differentiate as the root of the hair itself. Above the papilla, only the cortex (**CO**) of the hair is clearly seen in this section. (X140; H&E)

(b) A hair root sectioned more transversely shows the same layers of the follicular sheath, but the layers of the hair root are now seen to include the medulla (**M**), cortex (**CO**), and cuticle (**CU**). Other labels are like those of part **(a)**. (X140; H&E)

(c) SEM of a similar specimen gives a different perspective on these layers, including the shingle-like nature of the thin cuticle surface (**CU**), and the small blood vessel (**BV**) and collagen bundles (**CB**) near the surrounding connective tissue sheath (**CTS**). Other labels are like those of **(a)**. (X2600)

(Figure 18–14c, used with permission from Kessel RG, Kardon RH. Tissues and Organs: A Text-Atlas of Scanning Electron Microscopy. *San Francisco, CA: W.H. Freeman & Co.; 1979.)*

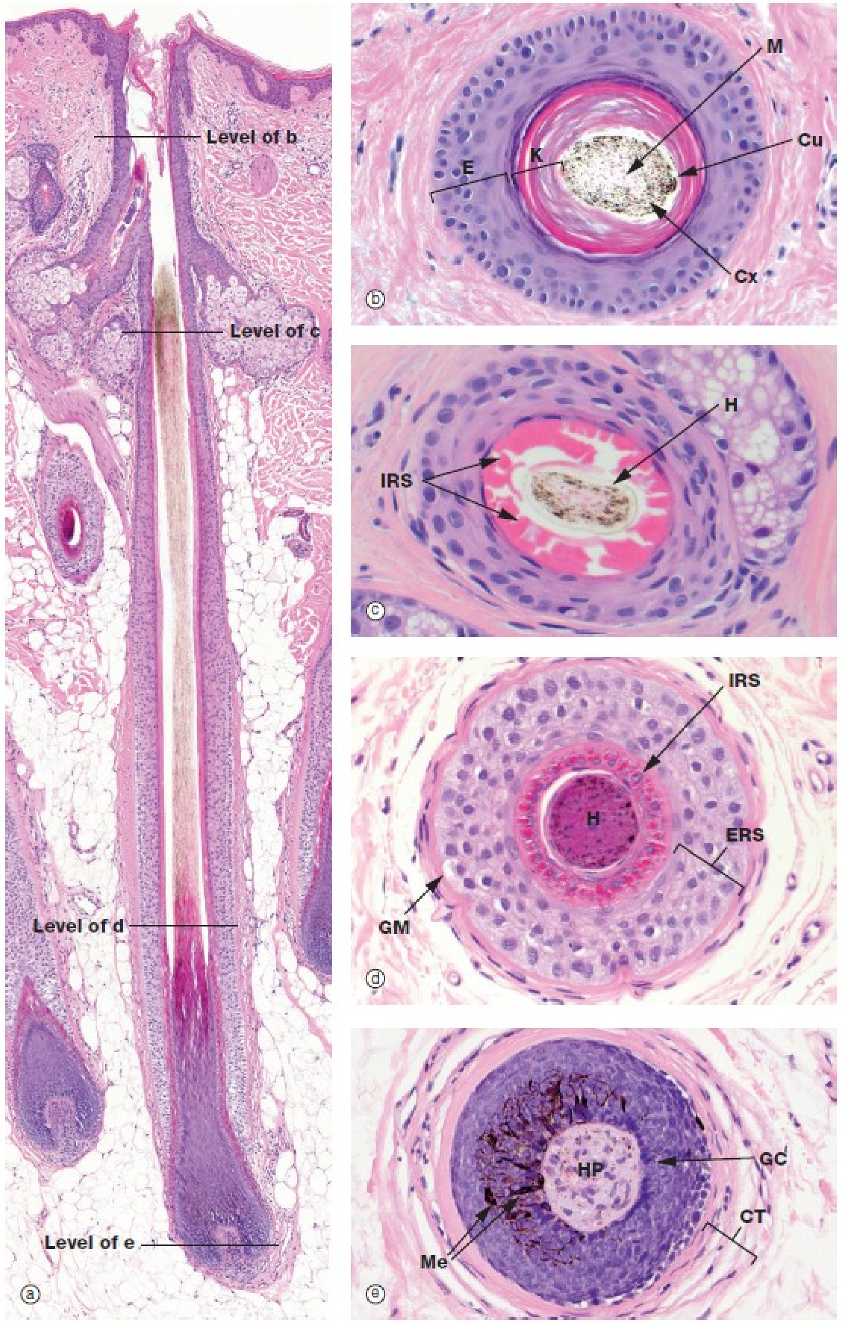


FIG. 9.10 Hair follicle *(caption and illustration (f) opposite)*
(a) H&E photomontage (LP) (b-e) H&E, TS (HP) (f) Diagram

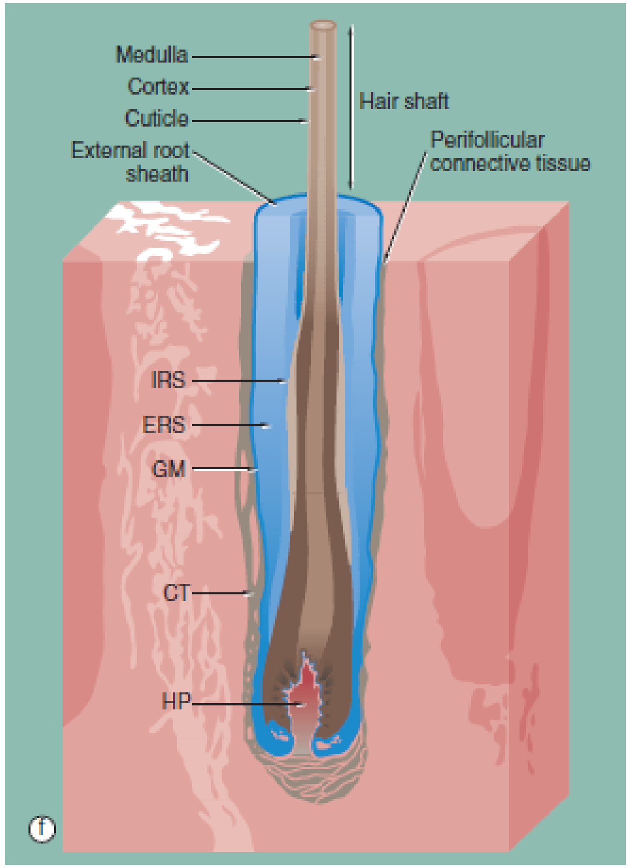


FIG. 9.10 Hair follicle *(illustrations (a-e) opposite)*
(a) H&E photomontage (LP) (b-e) H&E, TS (HP)
(f) Diagram

The hair follicle is a tubular structure formed of specialised peri-follicular connective tissue and epithelium. Micrograph (a) is a full-length image of a terminal scalp hair. At the base, there is a bulbous expansion, the hair bulb, enclosing the ***hair papilla*** **HP**.

During active hair growth, the epithelial cells around the hair papilla proliferate to form the layers of the follicle. In the hair bulb, all the layers start as an indistinguishable proliferative cell mass known as the ***hair matrix***. As they grow, they are pushed towards the skin surface from the hair bulb, and five epithelial layers form. The inner three epithelial layers undergo keratinisation to form the ***hair shaft*** (the hair) whilst the outer two layers form an internal and external sheath.

The cells of the innermost layer of the follicle undergo keratinisation to form the ***medulla*** **M** or core of the hair shaft; the medullary layer may not be distinguishable, especially in fine hairs. The medulla is surrounded by a broad, highly keratinised layer, the ***cortex*** **Cx**, which forms the bulk of the hair shaft. A third cell surface layer keratinises to form a hard, thin ***cuticle*** **Cu** on the surface of the hair, consisting of overlapping keratin plates, an arrangement which is said to prevent matting of the hair.

The outer fourth layer of the follicle constitutes the ***internal root sheath*** **IRS**; the cells of this layer become only lightly keratinised and lock with the developing cuticle, keeping the developing hair as a solid unit as it matures. After keratinisation, this layer fractures and fragments, leaving the hair shaft free in the follicle lumen, forming a space into which sebum is secreted around the maturing hair.

The outermost layer, the ***external root sheath*** **ERS**, is the external epithelial layer and merges with epidermis at the sebaceous glands. There is a thick, specialised basement membrane known as the ***glassy membrane*** **GM** and a surrounding specialised ***perifollicular connective tissue sheath*** **CT**.

Micrograph (e) shows a transverse section of the hair bulb, the distended base of the hair follicle, with an invaginated core of connective tissue, the hair papilla **HP**, containing small blood vessels and myelinated and non-myelinated nerve twigs. This is surrounded by a basal layer of palisaded active ***germinative cells*** **GC**. This germinative epithelium forms the follicle. In active (anagen) growth, the hair bulbs are prominent, with a well-formed hair papilla, and are located in subcutis.

In people with dark-coloured hair, melanocytes **Me** (see Fig. 9.6) are scattered amongst the proliferating cells of the hair bulb, with melanin being incorporated in the cells which will form the hair shaft. Black, brown and yellow forms of melanin are produced in various combinations and determine final hair colour.

Micrograph (d) is a transverse section through the hair follicle at the level shown by the line. The external root sheath **ERS** is separated from the connective tissue sheath **CT** by the glassy membrane **GM**. Passing inwards, the outermost cells, the external root sheath, have a homogeneous appearance. The internal root sheath **IRS** is recognised by its prominent, coarse, eosinophilic (***keratohyaline***) granules. Centrally is the hair shaft **H**.

In micrograph (c) at the level of sebaceous glands, the hair shaft is mature with a thin, pale-stained cuticle layer **Cu** which surrounds the pigmented cortex **Cx** and pale medulla **M**. The internal root sheath has now keratinised and is fragmenting as it is no longer required to support the developing hair shaft **H**, while the external root sheath is replaced by epidermis **E**.

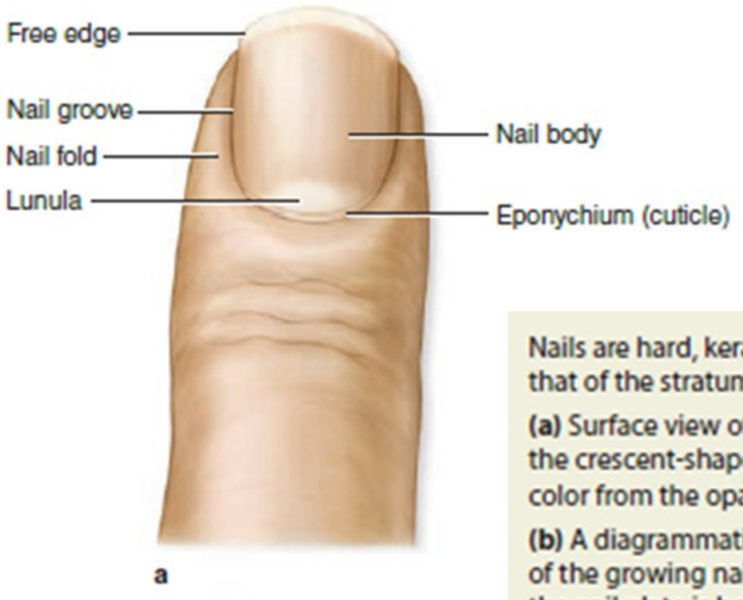
Micrograph (b) is above the sebaceous glands. This part of the follicle is called the ***follicular infundibulum***. It shows the hair shaft surrounded by epidermal-type keratin and epidermis. Note that the hair shaft is out of the plane of section in micrograph (a) at this level.

Each pilosebaceous follicle has an attached small smooth muscle called an ***arrector pili muscle*** (see Fig. 9.11).

SKIN

STRUCTURES ASSOCIATED WITH THE SKIN

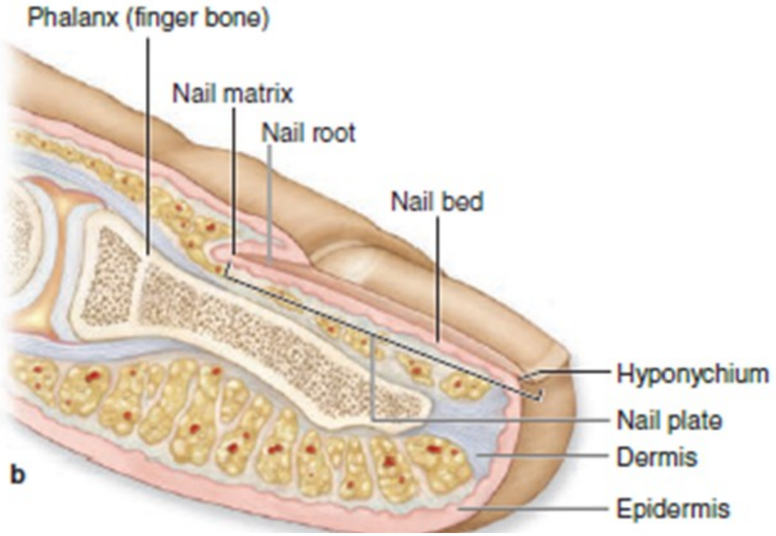
- **Nails**
  - Keratinized epithelial cells on the dorsal surface of the fingers and toes
  - Consist of a *nail plate* that corresponds to the stratum corneum of the epidermis. This plate rests on the *nail bed*, consisting of cells corresponding to the stratum spinosum and stratum germinativum.
  - *Nail root* lies in an epidermal fold, whose stratum corneum forms the *eponychium* (cuticle)
  - *Nail matrix* lies beneath the nail root and is the germinative portion of the nail.
  - The *hyponychium*, a thickened epidermis, secures the nail at the fingertip

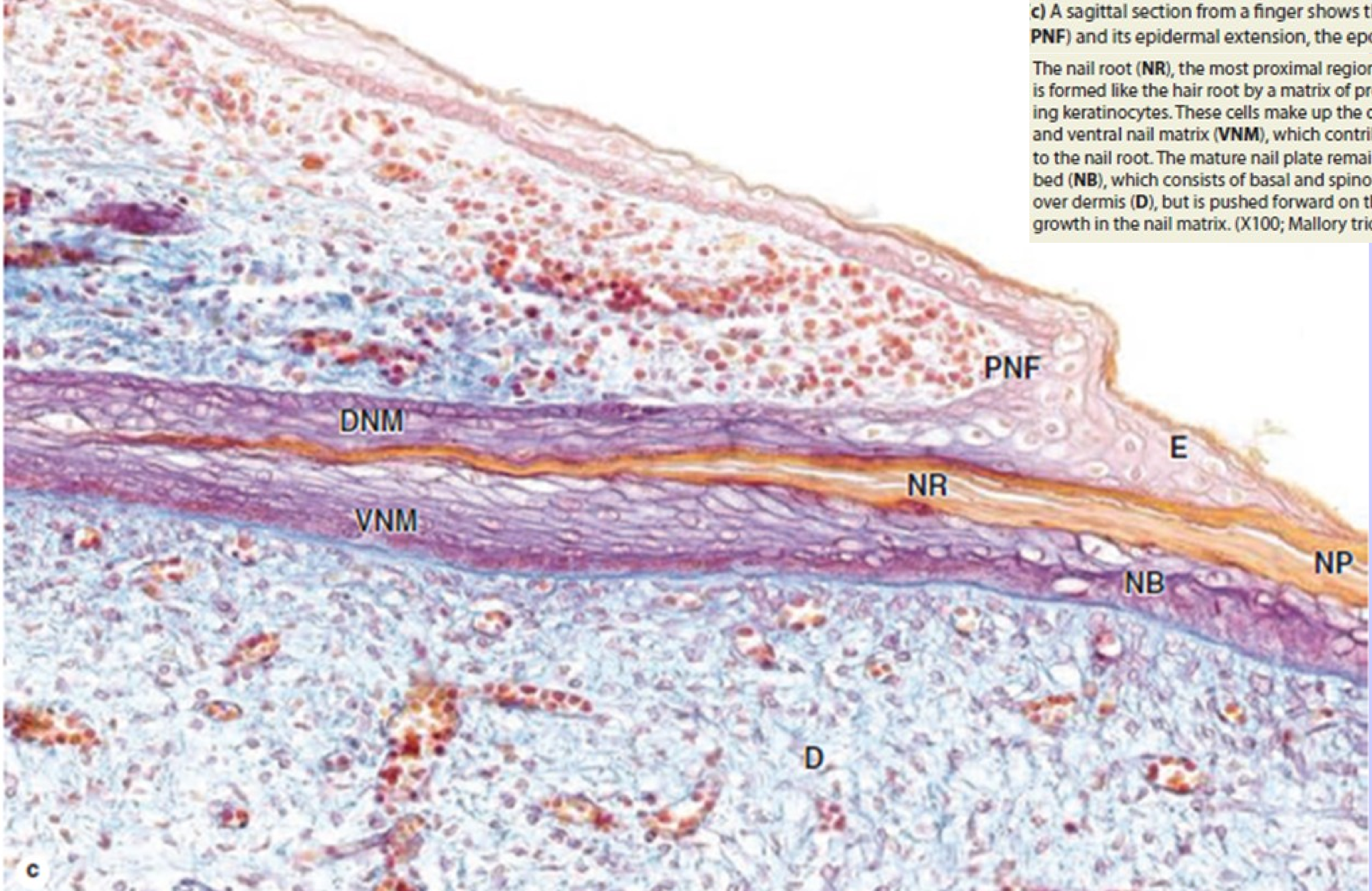


Nails are hard, keratinized derivatives formed in a process similar to that of the stratum corneum and hair.

(a) Surface view of a finger shows the nail's major parts, including the crescent-shaped white area called the **lunula**, which derives its color from the opaque nail matrix and immature nail plate below it.

(b) A diagrammatic sagittal section includes major internal details of the growing nail and the hyponychium where the free end of the nail plate is bound to epidermis.





c) A sagittal section from a finger shows the proximal nail fold (**PNF**) and its epidermal extension, the eponychium (**E**) or cuticle.

The nail root (**NR**), the most proximal region of the nail plate (**NP**), is formed like the hair root by a matrix of proliferating, differentiating keratinocytes. These cells make up the dorsal nail matrix (**DNM**) and ventral nail matrix (**VNM**), which contribute keratinized cells to the nail root. The mature nail plate remains attached to the nail bed (**NB**), which consists of basal and spinous epidermal layers over dermis (**D**), but is pushed forward on this bed by continuous growth in the nail matrix. (X100; Mallory trichrome)

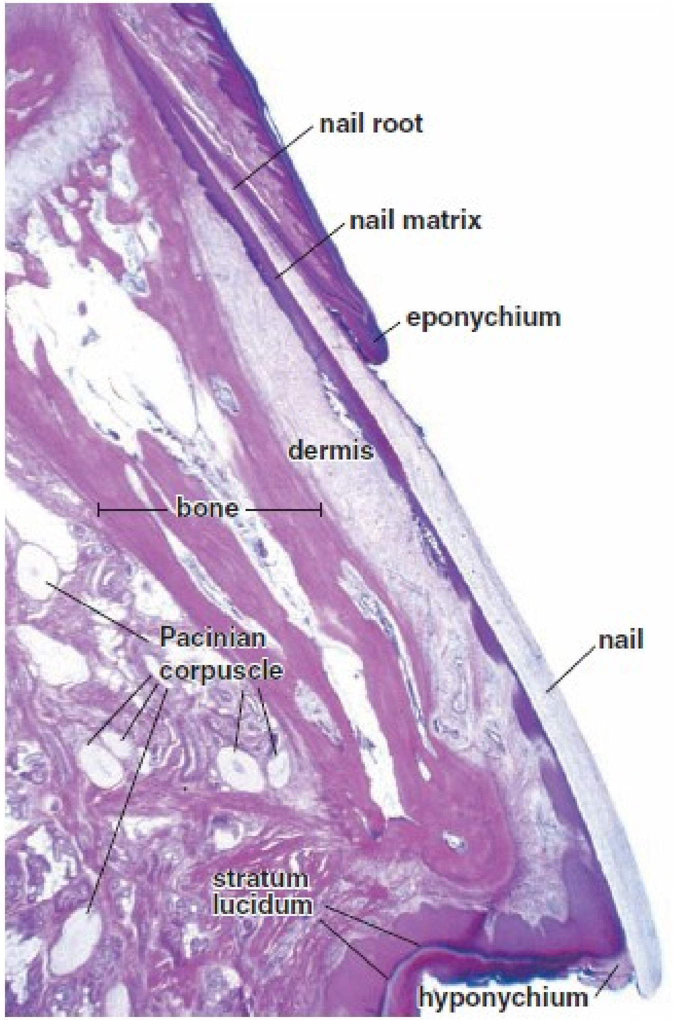
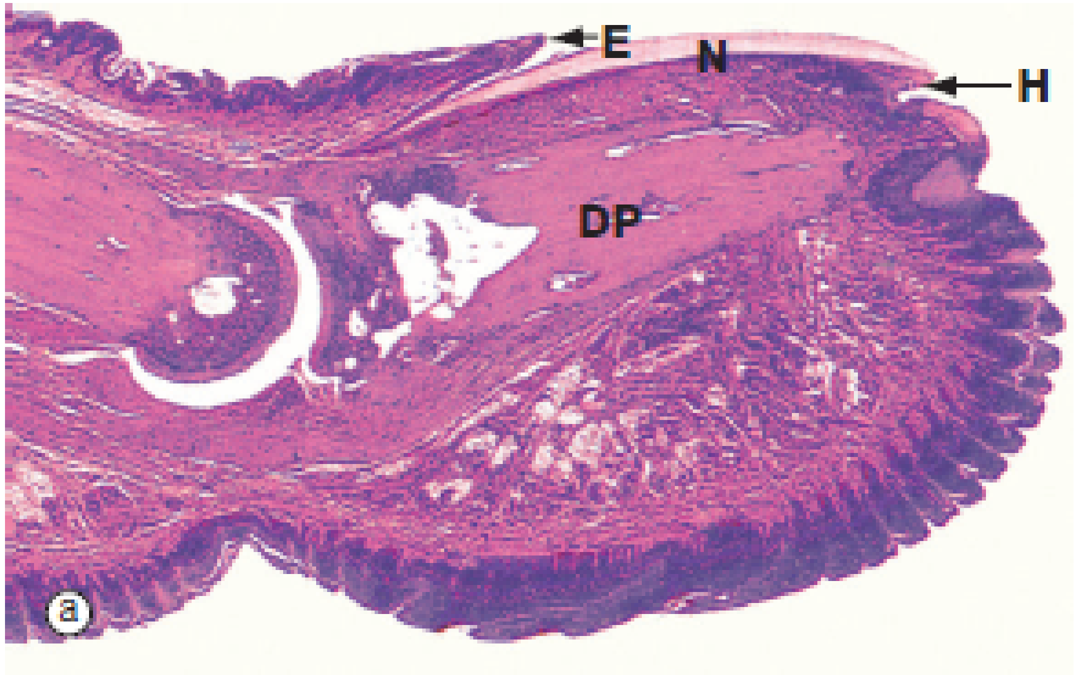


FIGURE 15.20 ▲ Photomicrograph of a sagittal section of distal phalanx with a nail. A nail is a keratinized plate located on the dorsal aspect of the distal phalanges. Under the free edge of the nail is a boundary layer, the hyponychium, which is continuous with the stratum corneum of the adjacent epidermis. The proximal end, the root of the nail, is overlapped by skin, the eponychium, which is also continuous with the stratum corneum of the adjacent epidermis. Deep to the nail is a layer of epithelium with underlying dermis. The proximal portion of this epithelium is referred to as the *nail matrix*. The bone in this section represents a distal phalanx. Numerous Pacinian corpuscles are present in the connective tissue of the palmar side of the finger. Note that even at this low magnification, the stratum lucidum is visible in the epidermis of the fingertip. ×10.



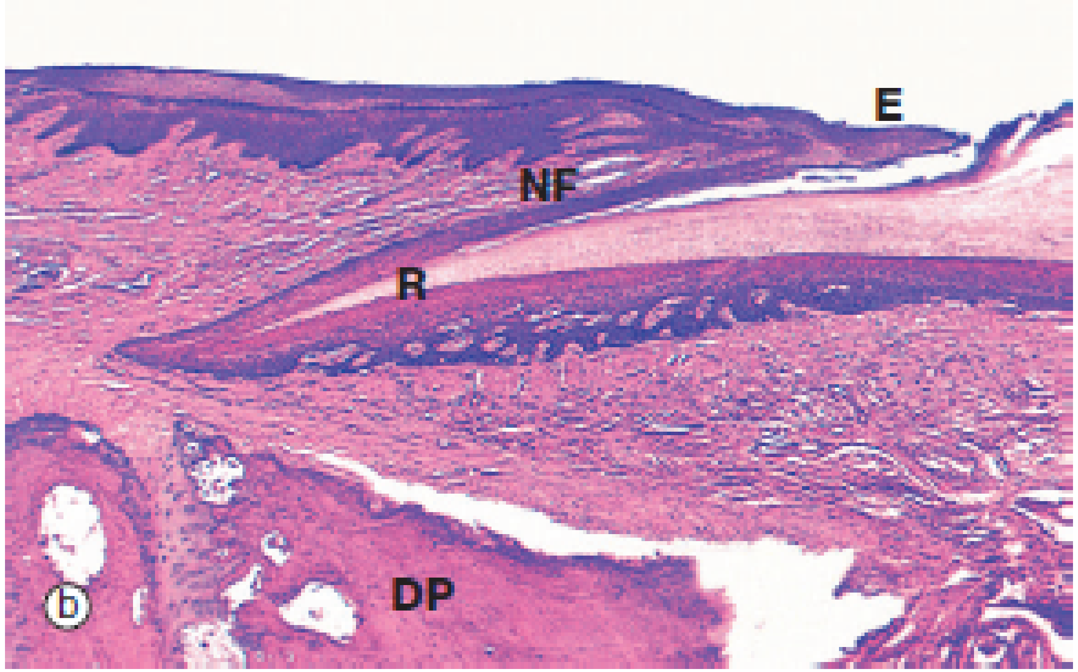


FIG. 9.9 Fingernail, monkey
(a) H&E (LP) (b) H&E (LP)

The dorsal skin surface of the tip of each finger and toe forms a highly specialised appendage, the nail, consisting of a dense keratinised plate, the ***nail plate*** **N**, which rests on a stratified squamous epithelium, the ***nail bed***. The proximal end of the nail, the ***nail root*** **R**, and the underlying nail bed extend deep into the dermis to lie in close apposition to the distal interphalangeal joint. The dermis beneath the nail plate is firmly attached to the periosteum of the ***distal phalanx*** **DP**.

Nail growth occurs by proliferation and differentiation of the epithelium underlying the nail root (known as the ***nail matrix***). The nail plate slides distally over the rest of the nail bed, which does not actively contribute to nail growth. Reflecting its proliferative activity, the nail matrix is thicker than the epithelium of the rest of the nail bed and exhibits pronounced epidermal ridges as seen in micrograph (b); on the surface, the distal part of the nail matrix is marked by the white crescent-shaped ***lunula*** at the base of the nail.

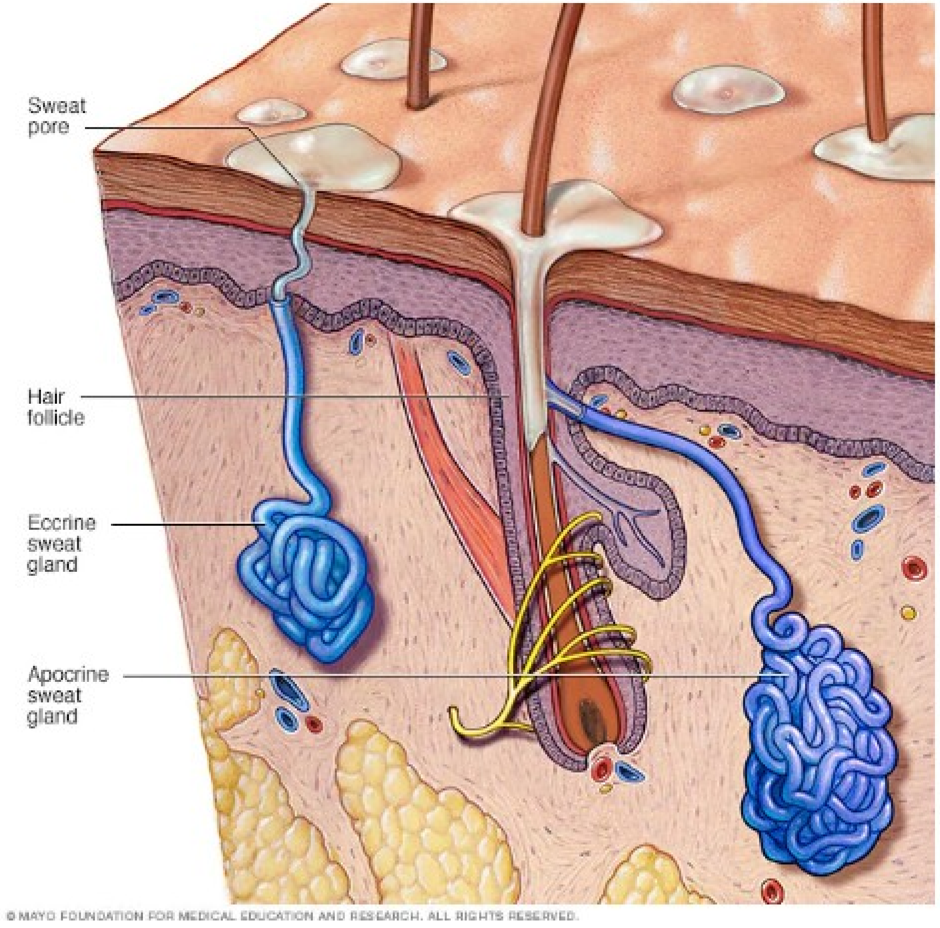
The skin overlying the root of the nail is known as the ***nail fold*** **NF** and its highly keratinised free edge is known as the ***eponychium*** **E**. The skin beneath the free end of the nail is known as the ***hyponychium*** **H**.

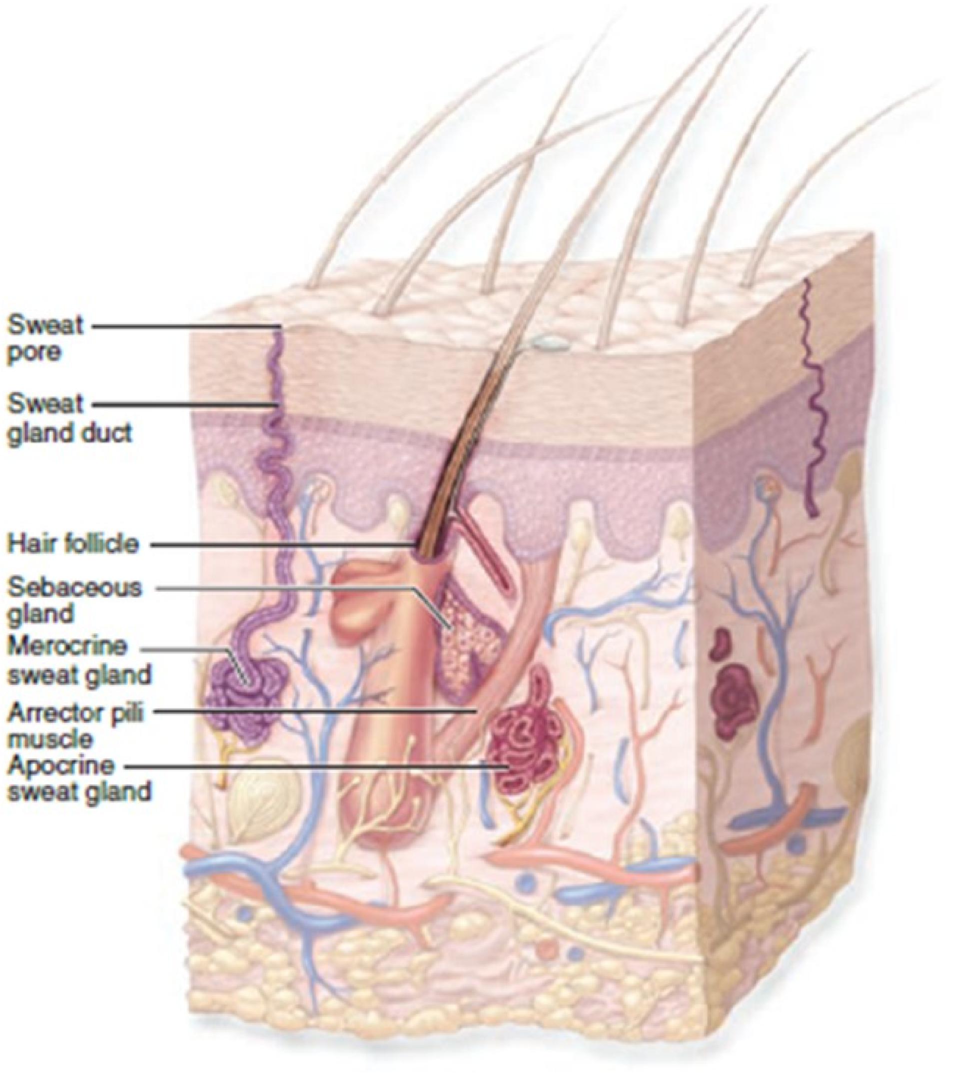
SKIN

STRUCTURES ASSOCIATED WITH THE SKIN

- **Sebaceous glands**
  - Simple, branched acinar glands
  - Usually secrete into a hair follicle
  - Produce sebum, an oily secretory product, released by the holocrine mode of secretion
  - Absent from thick skin

- **Sweat glands**
  - Simple, coiled tubular glands
  - Contain *myoepithelial cells*, which are specialized cells that contract to aid in the expulsion of the sweat
  - Types of sweat glands
    - *Merocrine or eccrine*. Located in all regions of the body except the axillary and anal regions; produce a watery secretion that empties onto the surface of the epidermis
    - *Apocrine*. Restricted to the axillary, areolar, and anal regions; much larger than eccrine sweat glands with a broader lumen. Produce a viscous secretion that empties into the hair follicle.





Skin includes three major types of exocrine glands. **Sebaceous glands** are usually part of a pilosebaceous unit with a hair follicle and secrete oily sebum into the space around the hair root. Thermoregulatory **eccrine sweat glands** empty their secretion onto the skin surface via sweat pores. **Apocrine sweat glands** secrete a more protein-rich sweat into the follicles of hair in skin of the axillae and perineum.

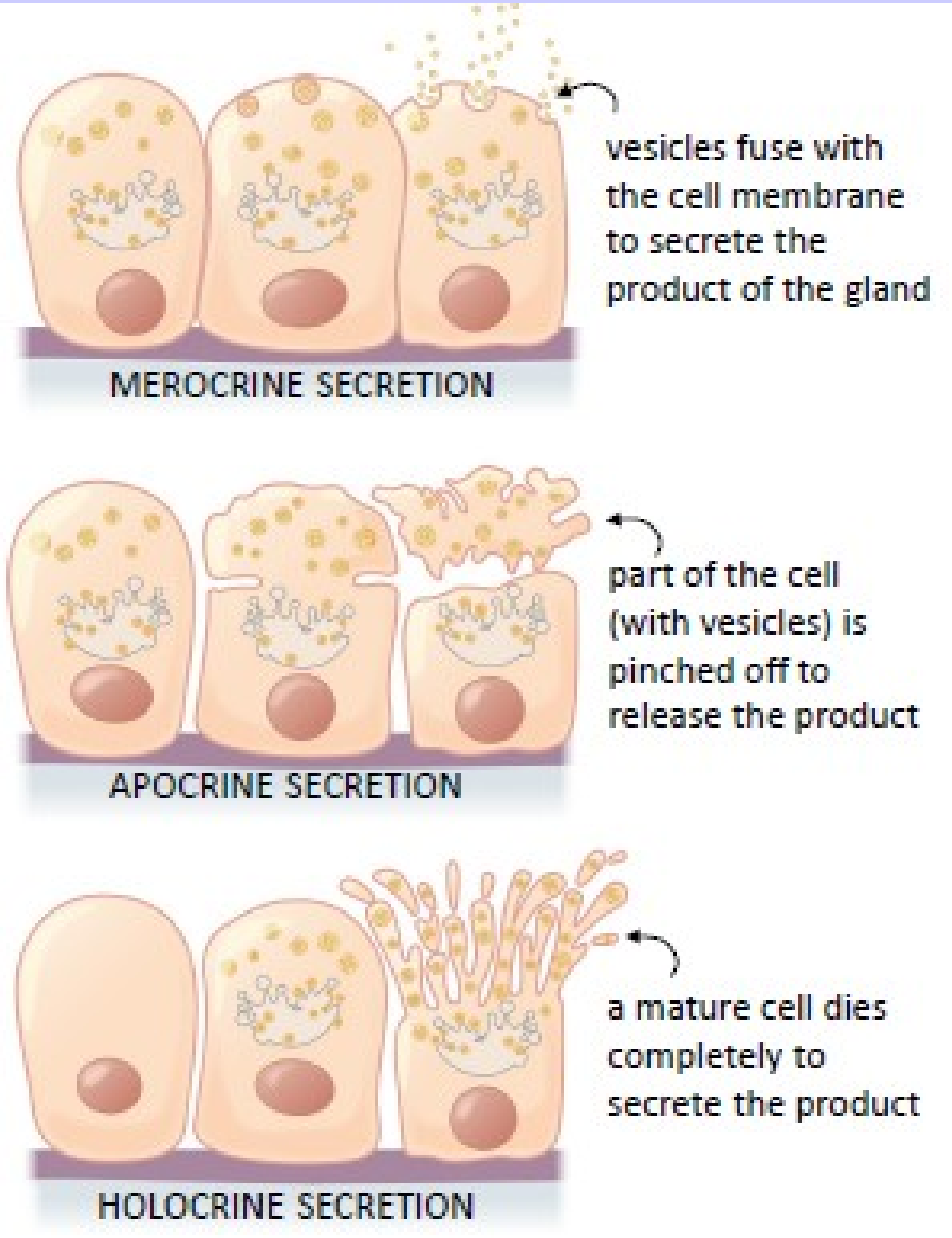
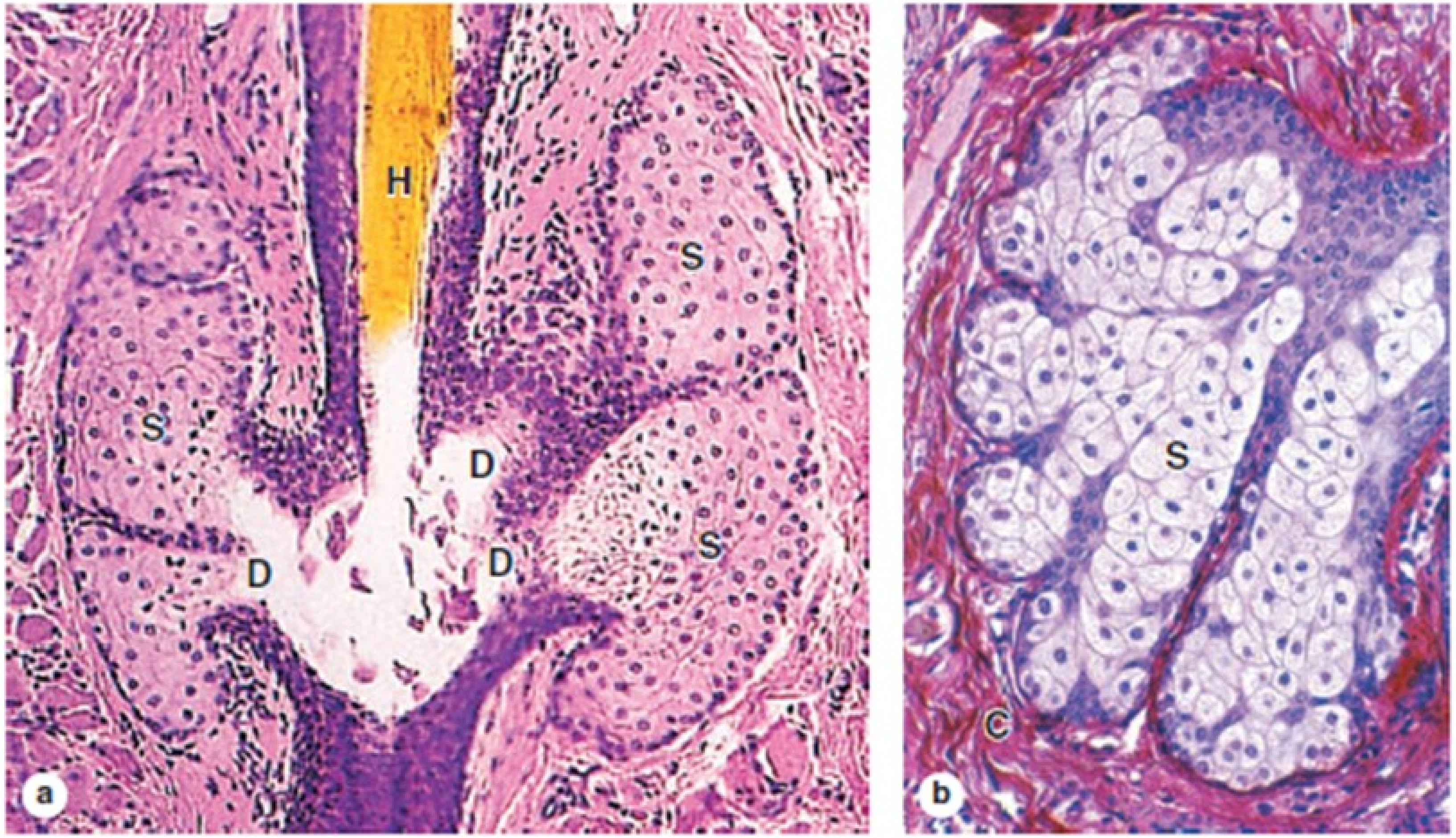


FIGURE 18–17 Sebaceous glands.



Sebaceous glands secrete a complex, oily mixture of lipids called **sebum** into short ducts, which in most areas open into hair follicles. Sebum production is the classic example of holocrine secretion, in which the entire cell dies and contributes to the secretory product.

(a) A section of a pilosebaceous unit shows acini composed of large sebocytes (**S**), which undergo terminal differentiation by filling with small lipid droplets and then disintegrating near the ducts (**D**) opening at the hair (**H**) shaft. (X122; H&E)

(b) A micrograph shows the gland's capsule (**C**) and differentiates sebocytes (**S**) at higher magnification. Proliferation of the small progenitor cells just inside the capsule continuously forces sebum into the ducts; myoepithelial cells are not present. (X400; H&E)

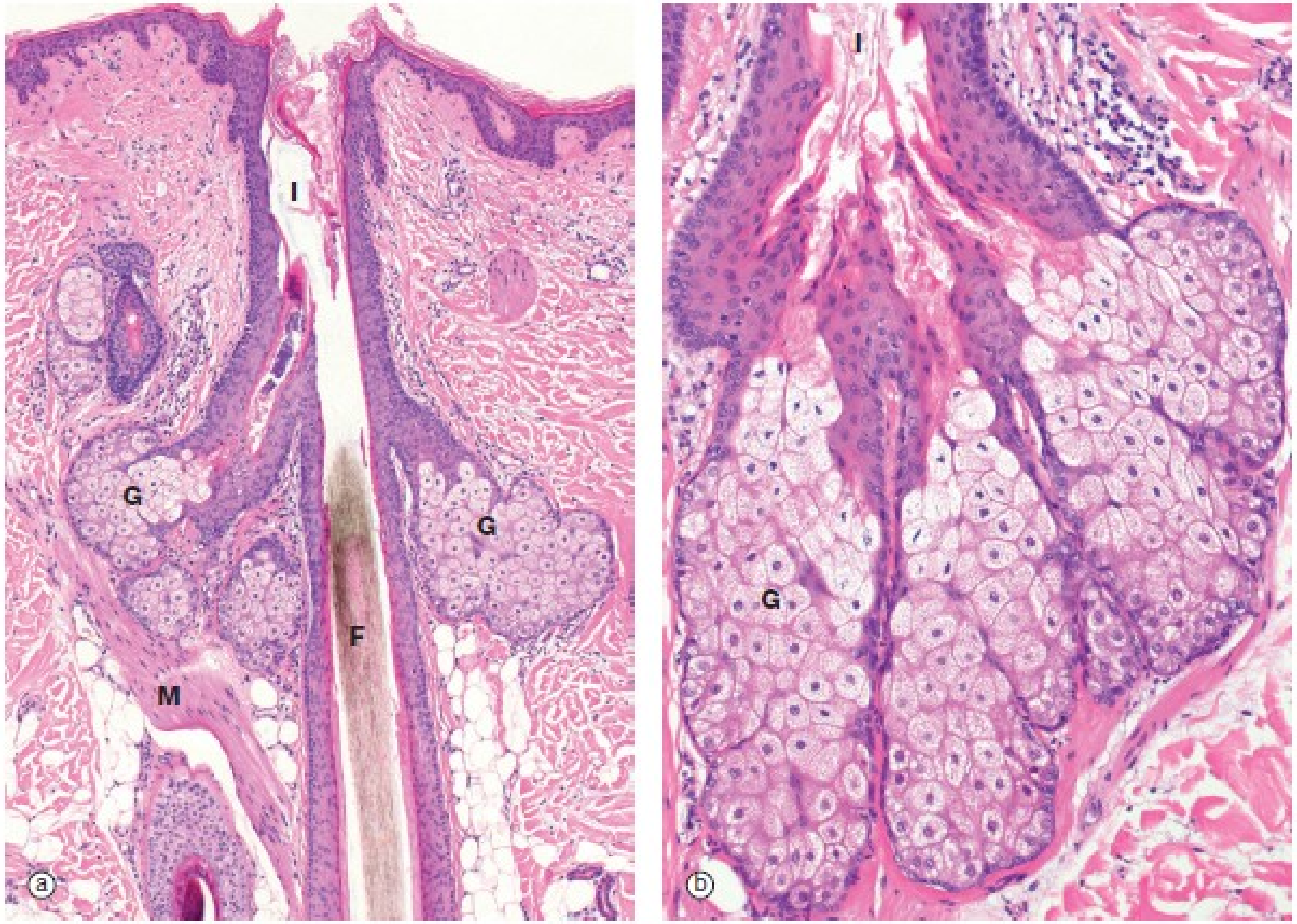


FIG. 9.11 Sebaceous glands and arrector pili
(a) H&E (LP) (b) H&E (MP)

Micrograph (a) illustrates the relationship of a sebaceous gland G and an *arrector pili muscle* M to a hair follicle F. At about mid-dermis, each hair follicle is surrounded by sebaceous glands which discharge their secretions onto the hair follicle and thence onto the skin surface. The superficial part of the follicle is called the *infundibulum* I. Sebaceous glands lie within the fibrous sheath surrounding the hair follicle and the glandular epithelium represents an outgrowth of the external root sheath. Arrector pili bind to the follicle just below the sebaceous glands.

More detail of sebaceous gland structure can be seen in micrograph (b). Each sebaceous gland has a branched acinar form, the acini converging upon a short duct which empties into the hair follicle beside the hair shaft. Each acinus consists of a mass of rounded cells packed with lipid-filled vacuoles; during tissue preparation, the lipid is largely removed, leaving clear spaces in the cytoplasm of these cells. Towards the duct, the lipid content of the acinar cells increases and the distended cells degenerate, releasing their contents, sebum, into the duct. This process is known as *holocrine secretion* (see Ch. 5). Cells lost by holocrine secretion are replaced by mitosis in the basal layer of the acinus.

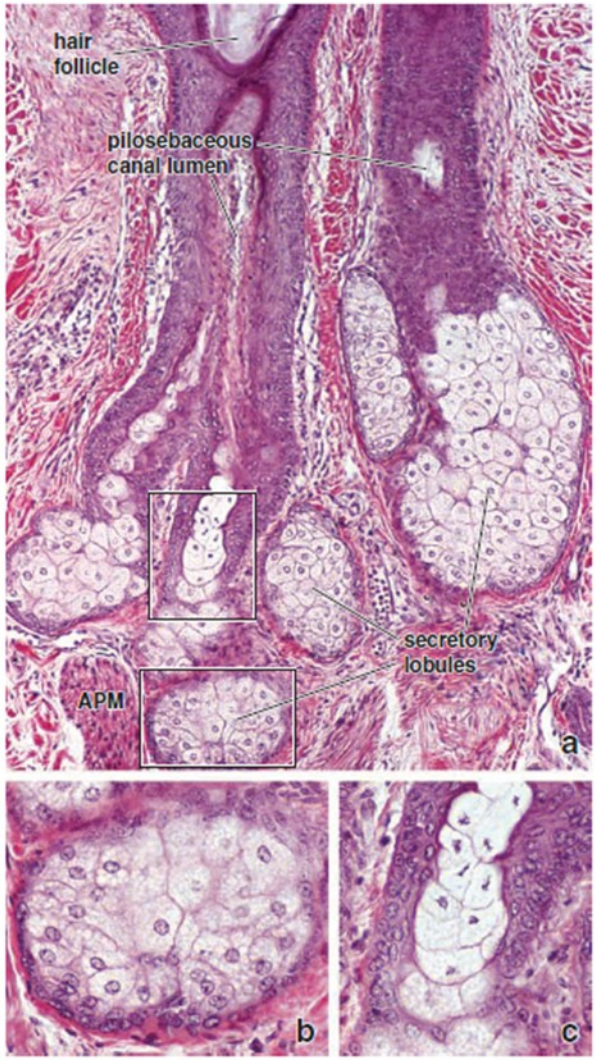
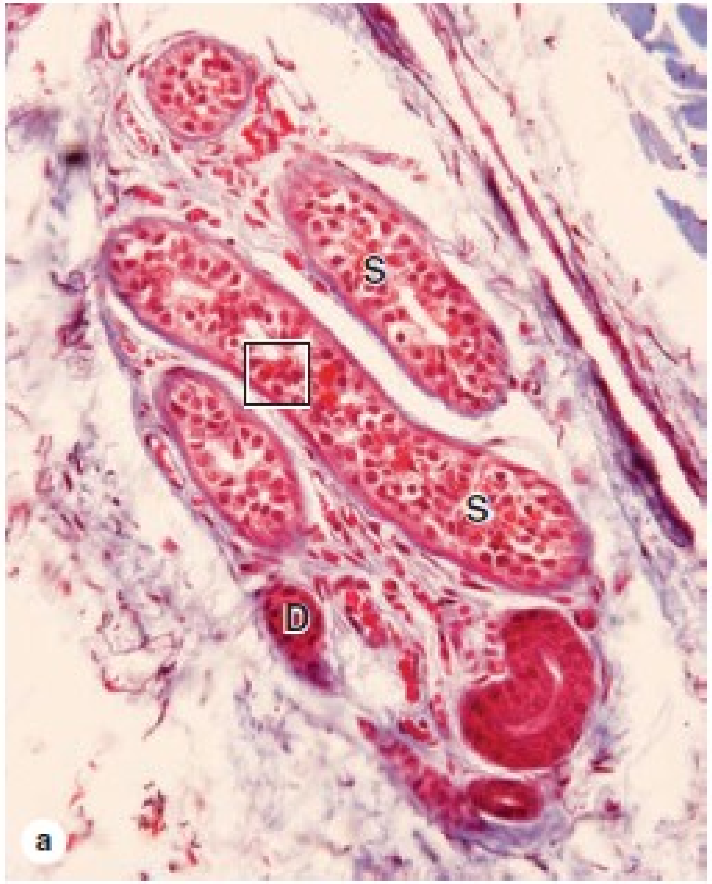
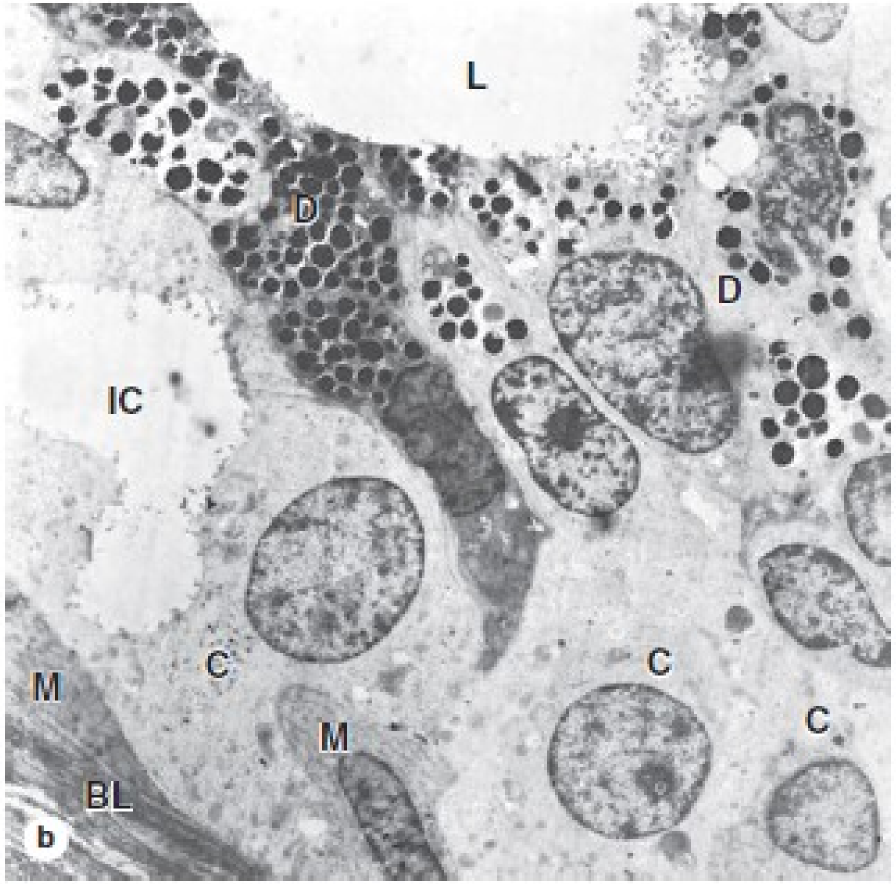


FIGURE 15.16 ▲ Photomicrograph of a sebaceous gland. a. This micrograph shows the secretory lobules and their pilosebaceous canal of two sebaceous glands. The canal of the gland on the *left* is about to enter the hair follicle seen at the *top* of the micrograph. The canal of the sebaceous gland on the *right* has been sectioned in a manner that shows mostly the wall of the canal. ×60. **b.** The secretory component of the lobule in the *lower box* of **a** is shown here at higher magnification. Note the light staining of the secretory cells due to the lack of staining of the sebum that they contain. These cells are actively producing sebum. The basal cells at the periphery of the lobule divide and replenish the population of new sebum-producing cells. Also, the arrector pili muscle (*APM*) composed of smooth muscle fibers is visible in the periphery of the secretory lobule. ×120. **c.** The secretory component of the lobule in the upper box of **a** is shown here at higher magnification. The sebum-filled cells are now within the canal. Note their pyknotic nuclei, signifying the death of the cell. ×120.

FIGURE **18–18** **Eccrine sweat glands.**





(a) Histologically eccrine glands have small lumens in the secretory components (**S**) and ducts (**D**), both of which have an irregular stratified cuboidal appearance. Both clear and acidophilic cells are seen in the stratified cuboidal epithelium of the secretory units. The box indicates an area with such cells like that shown ultrastructurally in part (b). (X200; Mallory trichrome)

(b) TEM of these important thermoregulatory structures reveals three cell types in their secretory portions. Myoepithelial cells (**M**) are present at the basal lamina (**BL**) to propel sweat into the duct. Irregular pyramidal cells called **dark cells** (**D**) border the lumen (**L**) and are filled with the electron-dense, eosinophilic secretory granules that release bactericidal peptides and other components of innate immunity. Columnar or cuboidal clear cells (**C**) on the basal lamina rapidly transport water from interstitial fluid in the capillary-rich dermis directly into the lumen or into intercellular canaliculi (**IC**) continuous with the lumen. Na^+ ions are recovered from this fluid through the action of cells in the ducts. (X6500)

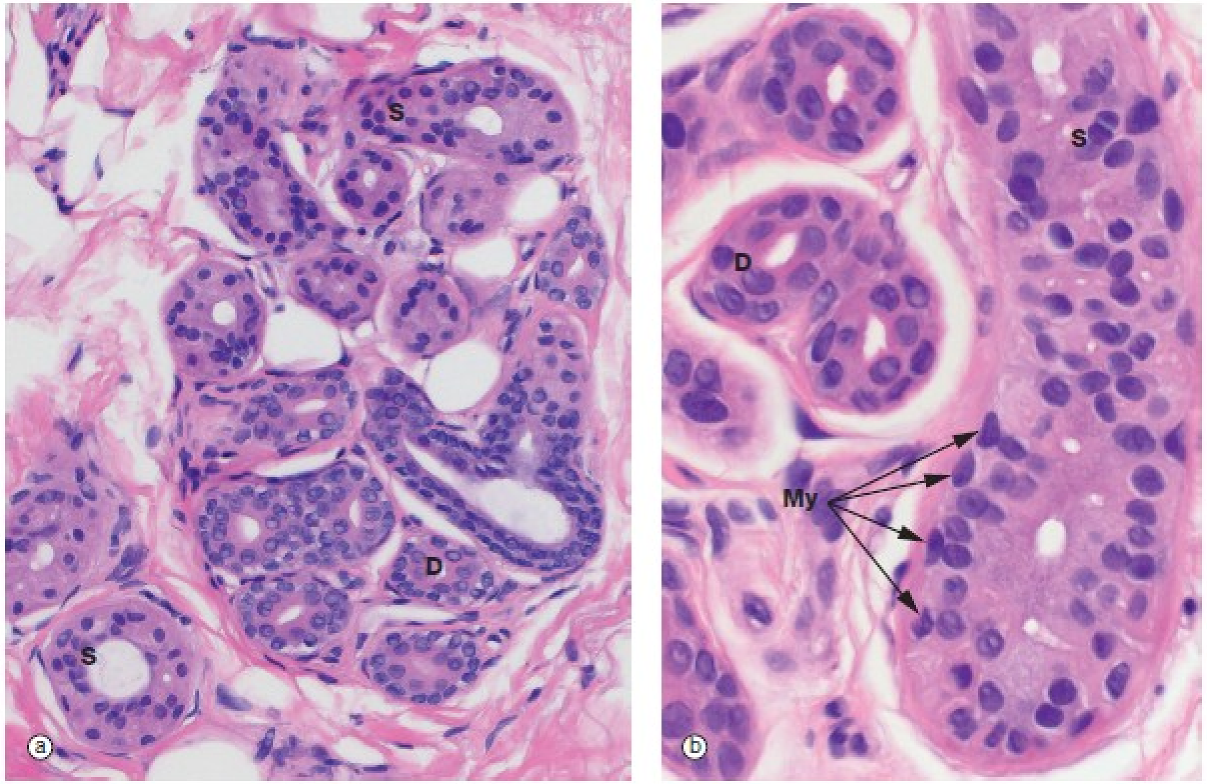


FIG. 9.12 Eccrine sweat glands and ducts
(a) H&E (MP) (b) H&E (HP)

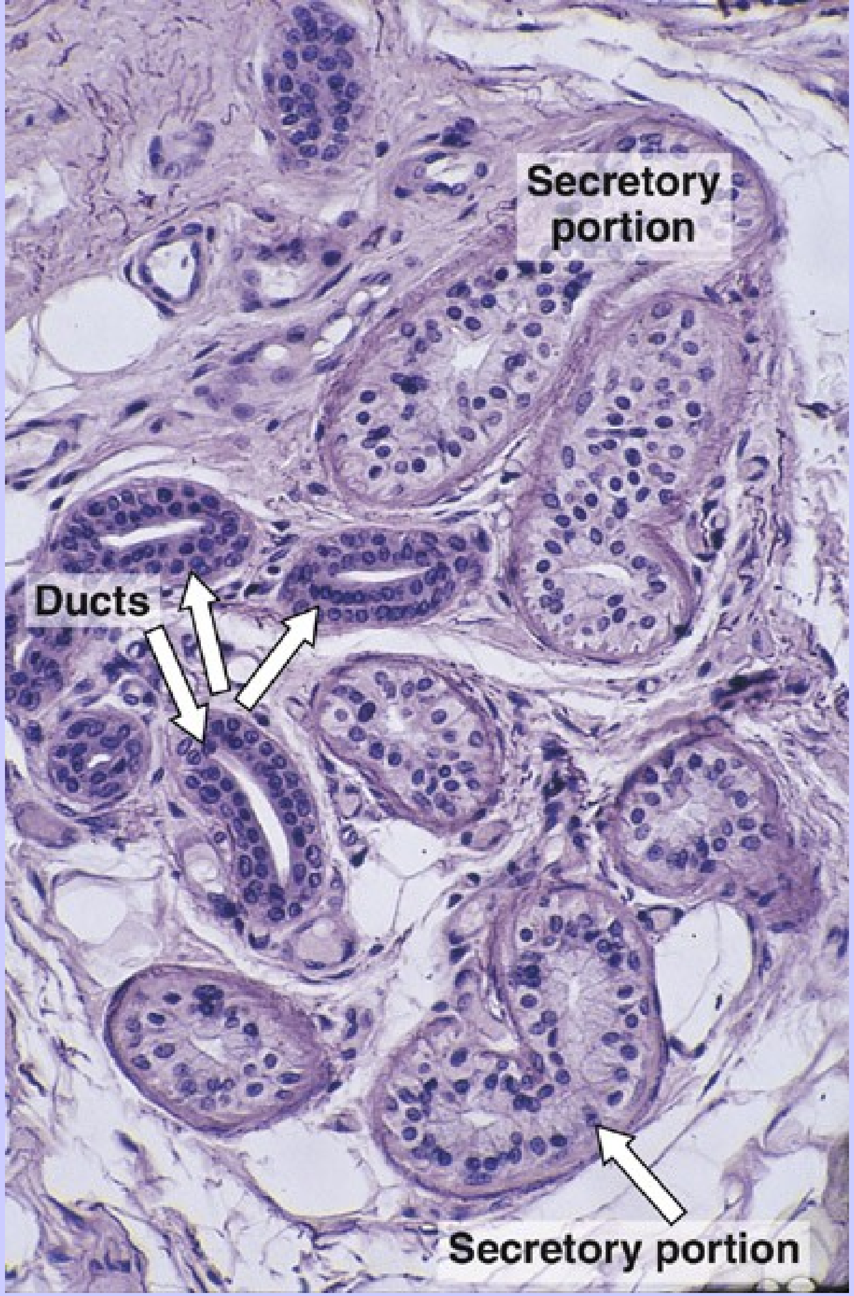
Eccrine glands occur everywhere in the skin and are particularly frequent on the palms, soles, forehead and axillae. They arise as downgrowths from the epidermis during the second trimester of intrauterine life and their function is to secrete sweat. The evaporation of sweat provides a means of lowering body temperature and is an important component of the thermoregulatory system. In addition to water, sweat contains significant quantities of sodium and chloride ions, some other ions, urea and some low molecular weight metabolites.

Histologically, an eccrine gland has two main components. The ***secretory component*** is a coiled secretory gland situated in the deep reticular dermis; the secretions formed there are passed into a coiled ***eccrine duct*** close to the secretory gland. The duct then becomes straight as it ascends vertically through the dermis towards the skin surface.

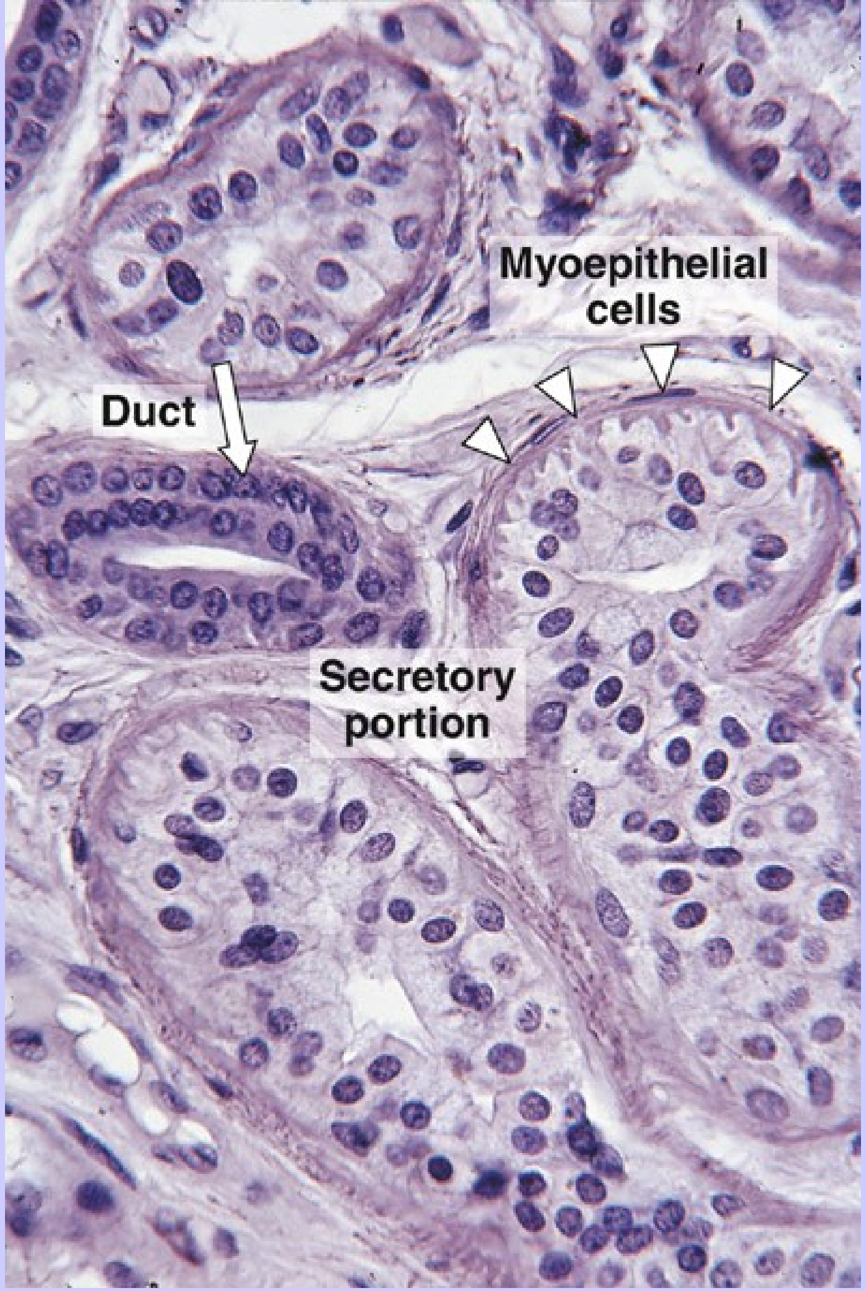
The secretory gland component **S** has an inner layer of large columnar or pyramidal cells with central oval nuclei and pale eosinophilic cytoplasm, interspersed with smaller, rarer darker-staining, cells best identified by a specific stain for mucopolysaccharides such as the PAS reaction. The clear cells secrete the bulk of the watery sweat and the smaller cells secrete a glycoprotein. The lateral walls of the secretory cells show prominent interdigitations which separate in places to form canaliculi that open into the gland lumen (not illustrated). These interdigitations greatly expand the area of the lateral plasma membrane, facilitating ion exchange.

The glands have an attenuated outer layer of contractile ***myoepithelial cells*** **My**, which form a discontinuous layer between the secretory cells and the basement membrane. They are spindle shaped and are arranged with their long axes tangential to the long axis of the coiled tubular gland.

The eccrine ducts **D** appear darker staining and have an obvious double layer of epithelial cells, the inner layer being larger and more cuboidal with microvilli lining the lumen. The luminal aspect often has a characteristic eosinophilic appearance (sometimes called the cuticle). This is partly due to the presence of a compact layer of circumferentially arranged tonofibrils in the cuboidal duct epithelial cells at the base of the abundant microvilli. The duct epithelium is biochemically active and modifies the composition of sweat, reabsorbing sodium ions.

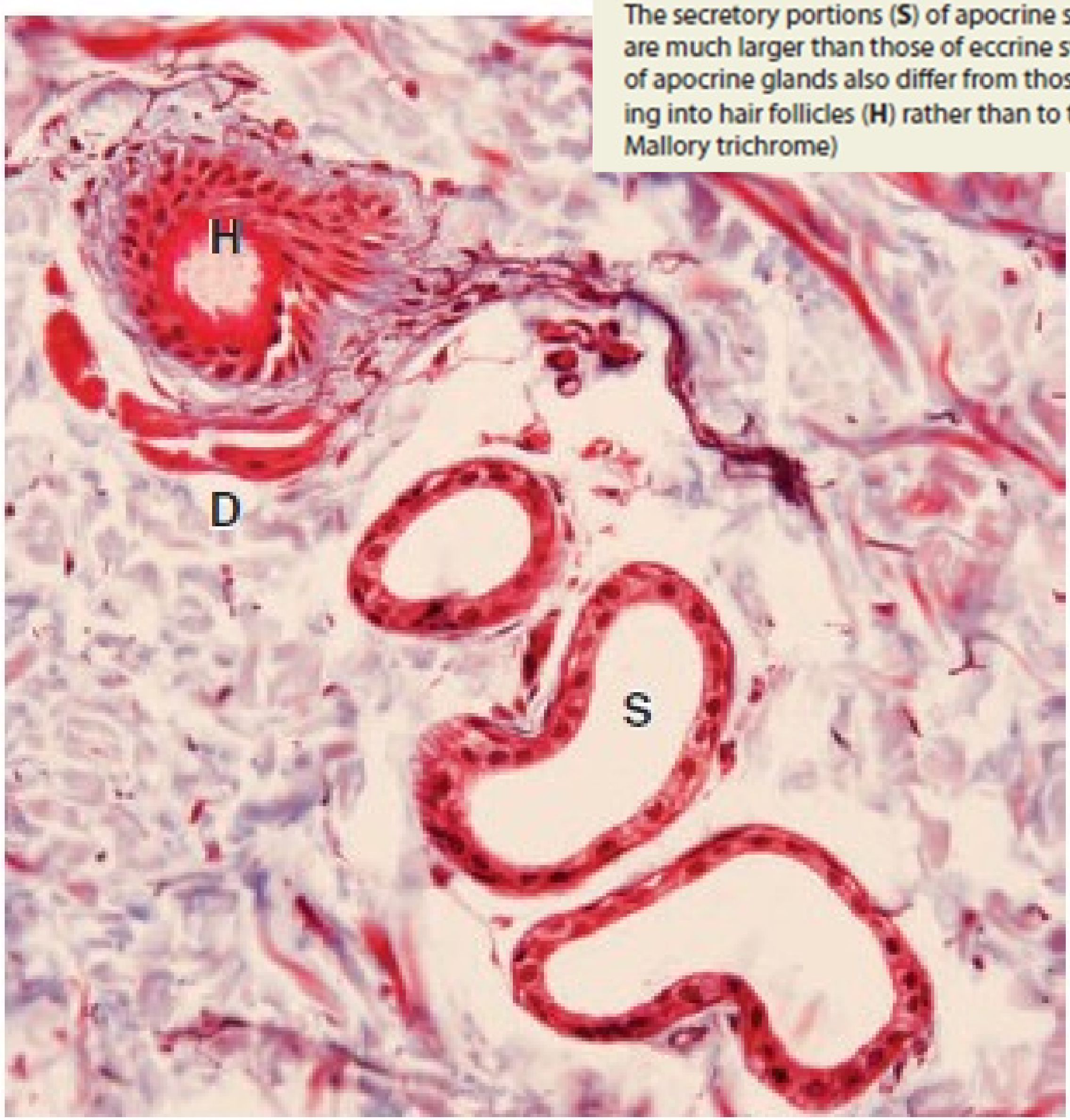


Sweet gland, simple coiled tubular gland. H&E stain



Sweet gland; the duct lined by stratified cuboidal epithelium; myoepithelial cells surround the secretory portion (contraction helps tho discharge the glandular secretion). H&E stain

FIGURE 18–19 Apocrine sweat glands.



The secretory portions (**S**) of apocrine sweat glands have lumens that are much larger than those of eccrine sweat glands. The ducts (**D**) of apocrine glands also differ from those of eccrine glands in opening into hair follicles (**H**) rather than to the epidermal surface. (X200; Mallory trichrome)

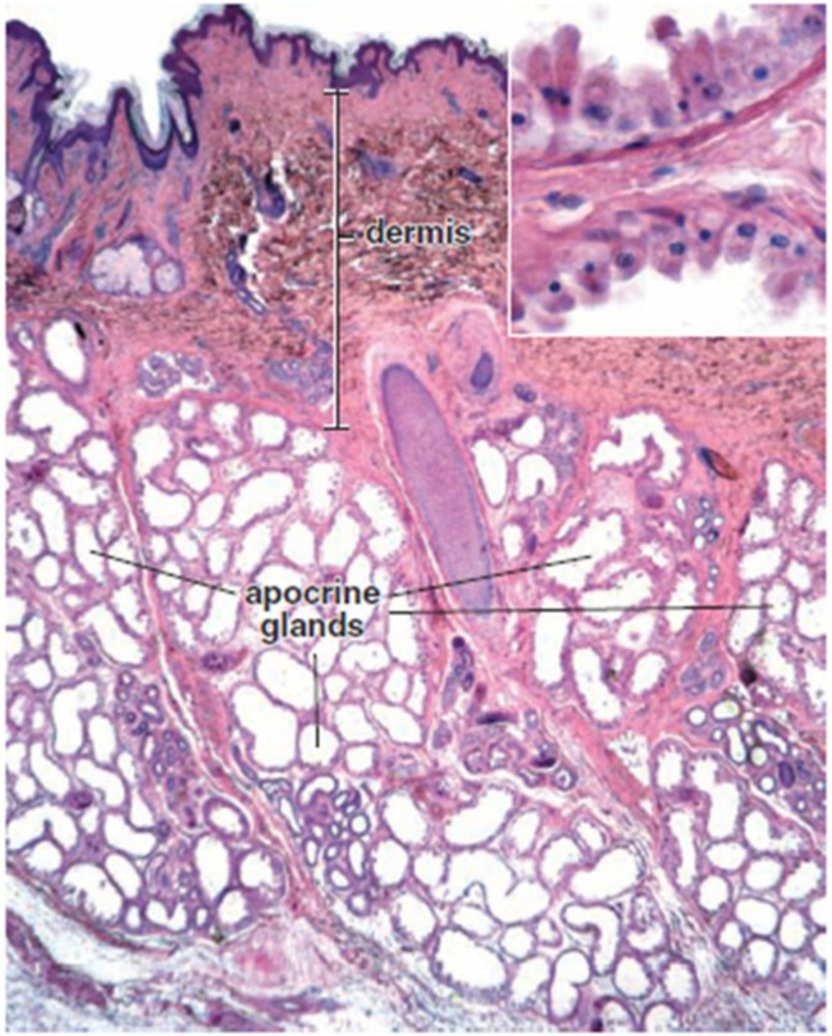


FIGURE 15.19 ▲ Photomicrograph of an apocrine sweat gland. This section of adult skin from the area around the anus shows several apocrine (anal) sweat glands, which are easily identified by the large lumen of their secretory components. This apocrine sweat gland is close to a hair follicle (*center* of photomicrograph) and deep to the dense, irregular connective tissue of the dermis. ×45. **Inset.** Higher magnification of secretory component shows the cell types of the apocrine gland. The gland consists of a simple epithelium whose cells are either cuboidal or columnar and myoepithelial cells located in the basal portion of the epithelial cell layer. ×230.

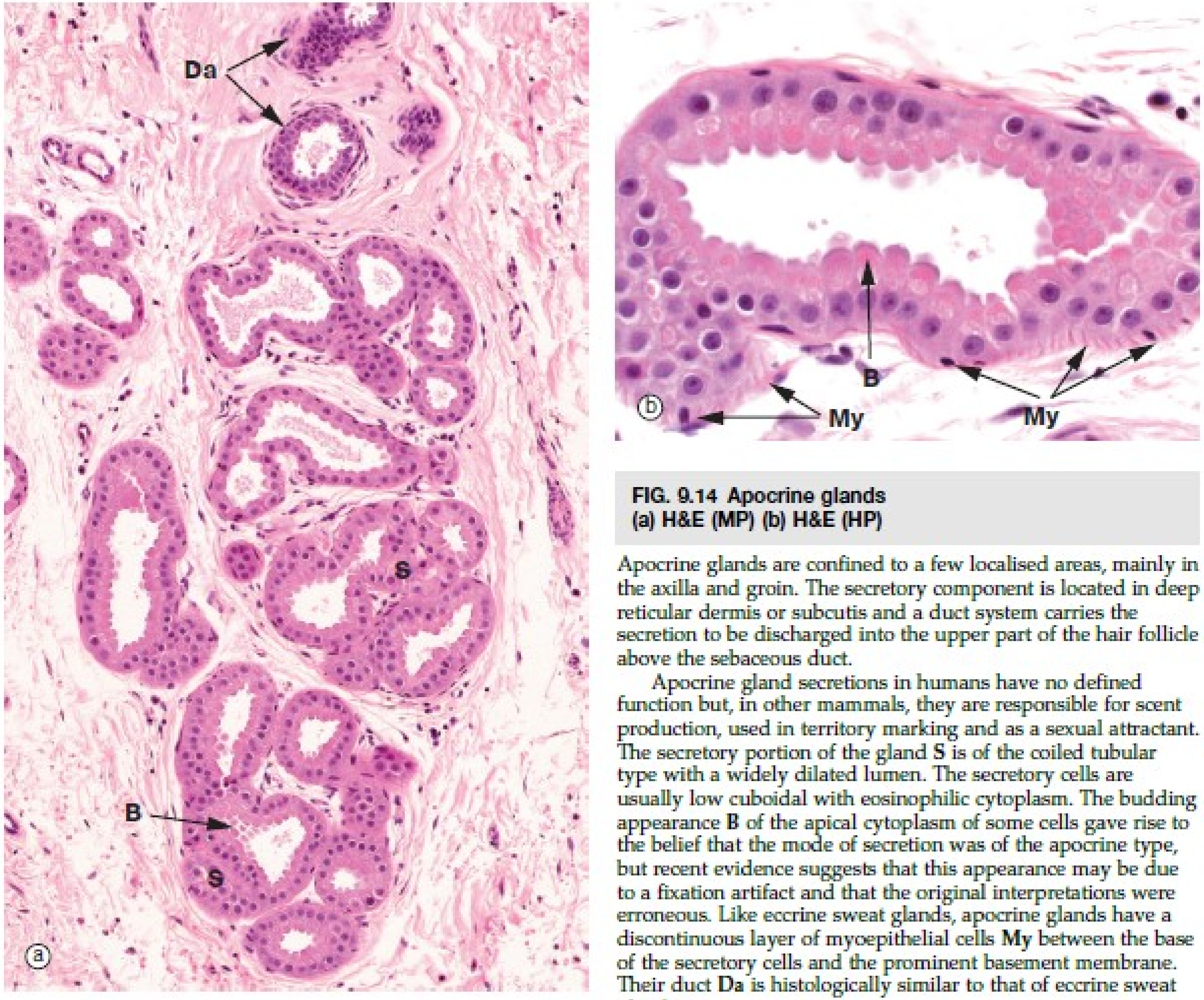


FIG. 9.14 Apocrine glands
(a) H&E (MP) (b) H&E (HP)

Apocrine glands are confined to a few localised areas, mainly in the axilla and groin. The secretory component is located in deep reticular dermis or subcutis and a duct system carries the secretion to be discharged into the upper part of the hair follicle above the sebaceous duct.

Apocrine gland secretions in humans have no defined function but, in other mammals, they are responsible for scent production, used in territory marking and as a sexual attractant. The secretory portion of the gland **S** is of the coiled tubular type with a widely dilated lumen. The secretory cells are usually low cuboidal with eosinophilic cytoplasm. The budding appearance **B** of the apical cytoplasm of some cells gave rise to the belief that the mode of secretion was of the apocrine type, but recent evidence suggests that this appearance may be due to a fixation artifact and that the original interpretations were erroneous. Like eccrine sweat glands, apocrine glands have a discontinuous layer of myoepithelial cells **My** between the base of the secretory cells and the prominent basement membrane. Their duct **Da** is histologically similar to that of eccrine sweat glands.

Apocrine glands do not become functional until puberty and, in women, undergo cyclical changes under the influence of the hormones of the menstrual cycle.

TABLE 9.1 Review of skin

Major structures	Main structures or cells	Brief description/function
Epidermis • Keratin layer • Granular cell layer • Prickle cell layer • Basal cell layer	Keratinocytes	Proliferate from base, move upward and keratinise to form a non-living protective, abrasion resistant waterproofing keratin layer, the stratum corneum
	Melanocytes	Basally located; produce melanin pigment and pass to keratinocytes; provide UV light protection
	Langerhans cells	Antigen presenting cells throughout epidermis (and superifical dermis)
	Merkel cells	Basally located sensory neuroendocrine cells
	Basement membrane, the dermo-epidermal junction	Specialised structure produced by epidermis and dermis in combination; ties the epidermis to dermis
Dermis	Collagen and elastin	Provide strength and elasticity
	Vessels • Papillary/superficial plexus • Cutaneous plexus • Glomus bodies	 Supplies dermal papillae and thus epidermis together with superficial dermis Supplies deep dermis and subcutis AV shunts; divert blood from skin to conserve heat; found mainly in hands, feet, ears
Adnexae	Nails	Keratin plates; strengthen tips of fingers and toes
	Pilosebaceous units • Hair follicles • Sebaceous glands • Arrector pili muscles	 Produces hair Sebum (oil) producing holocrine glands Follicle associated smooth muscle bundles
	Eccrine glands	Produce sweat, a critical means of body cooling
	Apocrine glands	Glands of groin and axilla; produce odour
Subcutis	Adipose tissue	Triglyceride (fat) store; provides insulation and structural padding
	Fibrous tissue septae	Strengthens the adipose tissue and ties subcutis to both dermis and underling structues such as fascias
Nerves	Meissner corpuscles	Papillary dermal touch receptors concentrated in hands and feet
	Merkel cell neurites	Papillary dermal touch receptors concentrated in hands and feet
	Free nerve endings	Pain and temperature receptors