General Human Histology

The Skin

Lec:1 ,2

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- The skin is the largest single organ of the body, typically accounting for 15-20% of total body weight and, in adults, presenting 1.5-2m^2 of surface to the external environment.
- Also known as the **integument** (L. *integumentum*, covering) or **cutaneous layer**,

the skin is **composed** of the epidermis, an epithelial layer of ectodermal origin, and the dermis, a layer of mesodermal connective tissue (Figure 18–1).

- At the irregular junction between the dermis and epidermis, projections called **dermal papillae** interdigitate with invaginating **epidermal ridges** to strengthen adhesion of the two layers.
- Epidermal derivatives include hairs, nails, and sebaceous and sweat glands.
- Beneath the dermis lies the **subcutaneous tissue** or **hypodermis**, a loose connective tissue layer usually containing pads of adipocytes

- The specific functions of the skin fall into several broad categories.

■ **Protective:** It provides a physical barrier against thermal and mechanical insults such as friction and against most potential pathogens and other material

- **Sensory:** Many types of sensory receptors allow skin to constantly monitor the environment, and various skin mechanoreceptors help regulate the body's interactions with physical objects.
- **Thermoregulatory:** A constant body temperature is normally easily maintained thanks to the skin's insulating components (eg, the fatty layer and hair on the head) and its mechanisms for accelerating heat loss (sweat production and a dense superficial microvasculature).

- **Metabolic:** Cells of skin synthesize vitamin D_3, needed in calcium metabolism and proper bone formation, through the local action of UV light on the vitamin's precursor. Excess electrolytes can be removed in sweat, and the subcutaneous layer stores a significant amount of energy in the form of fat.
- **Sexual signaling:** Many features of skin, such as pigmentation and hair, are visual indicators of health involved in attraction between the sexes in all vertebrate species, including humans. The effects of sex pheromones produced by the apocrine sweat glands and other skin glands are also important for this attraction.

Histology (structure)

Epidermis (thinner outer layer of skin)

Dermis (thicker connective tissue layer)

Hypodermis (subcutaneous layer)

- This system (integumentary) is divided into:

  1- skin

  2- hair

  3- glands

  4- nails

  5- nerve endings

  I) Skin

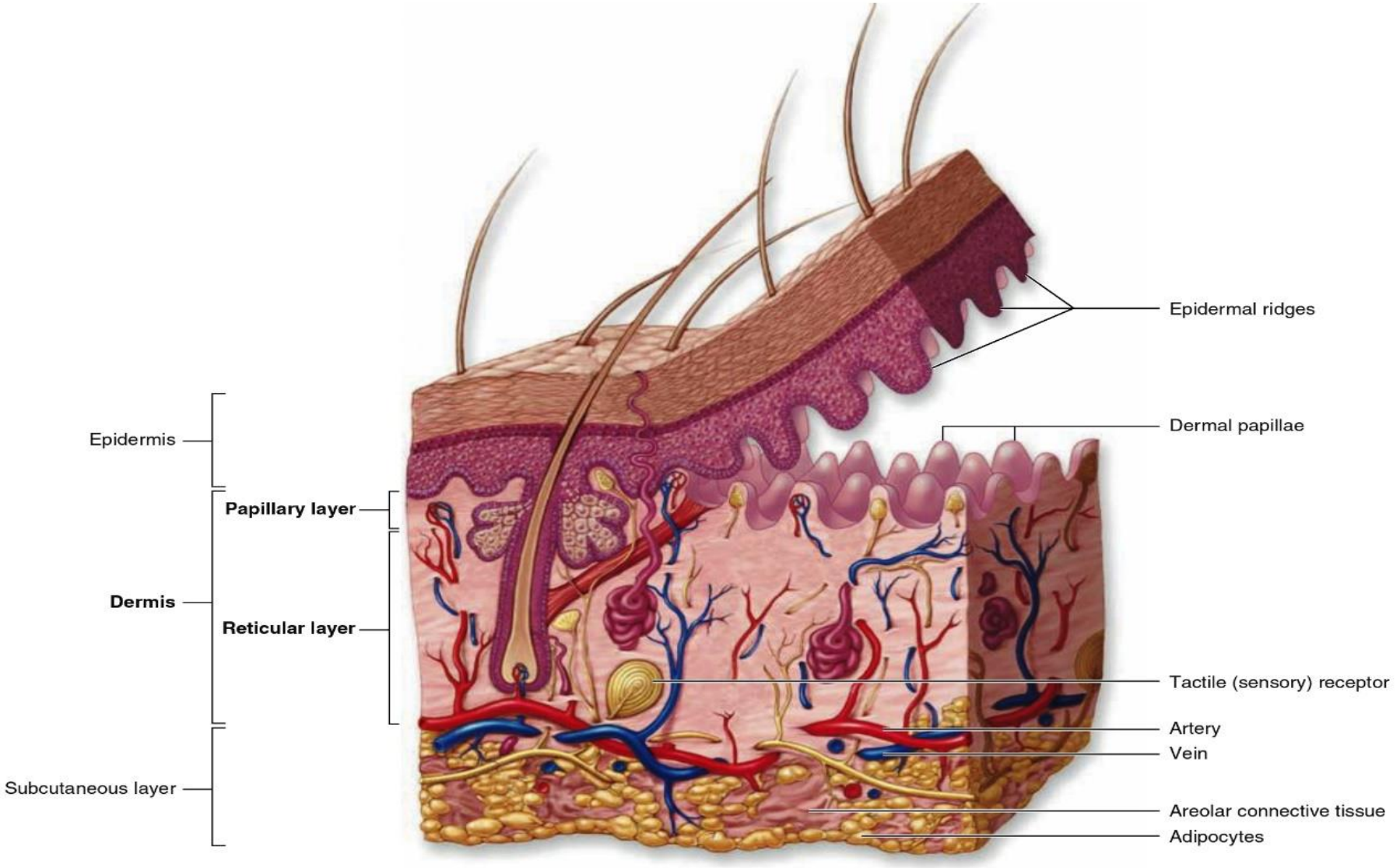
  Skin is an organ because it consists of different tissues that are joined to perform a specific function.

  Largest organ of the body in surface area and weight.

  Dermatology: is the medical specialty concerning the diagnosing and treatment of skin disorders.

- **The epidermis:**
- consists mainly of a stratified squamous keratinized epithelium composed of cells called **keratinocytes**.
- There are also three much less abundant epidermal cell types: pigment-producing **melanocytes**, antigen-presenting **Langerhans cells**, and tactile epithelial cells called **Merkel cells** (Figure 18–2).

- The epidermis forms the major distinction between **thick skin** (Figure 18–2a), found on the palms and soles, and **thin skin** (Figure 18–3) found elsewhere on the body.
- The designations “thick” and “thin” refer to the thickness of the epidermal layer, which alone varies from 75 to 150 μm for thin skin and from 400 to 1400 μm for thick skin.
- Total skin thickness (epidermis plus dermis) also varies according to the site. For example, full skin on the back is about 4-mm thick, whereas that of the scalp is about 1.5-mm thick.



Diagrammatic overview of skin, showing the major layers and epidermal appendages (hair follicles, sweat, and sebaceous glands), the vasculature, and the major sensory receptors.

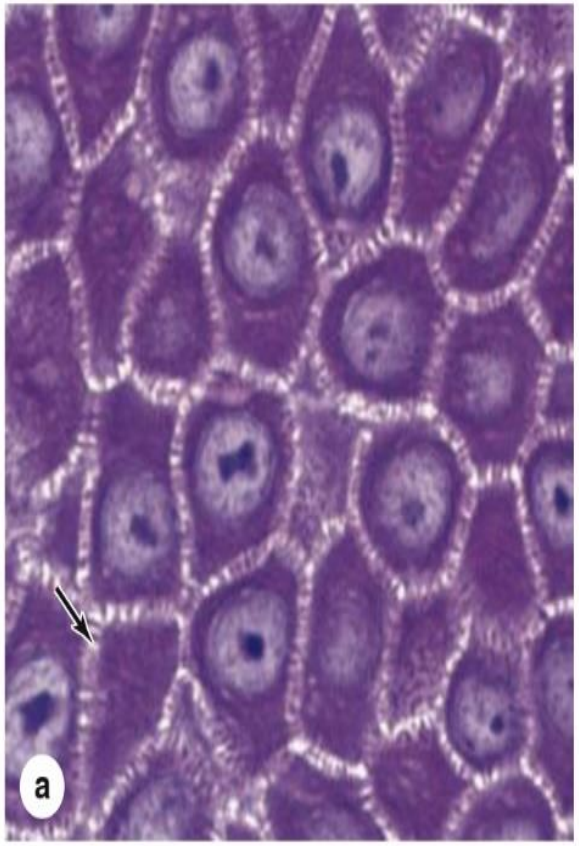
Layers and appendages of skin

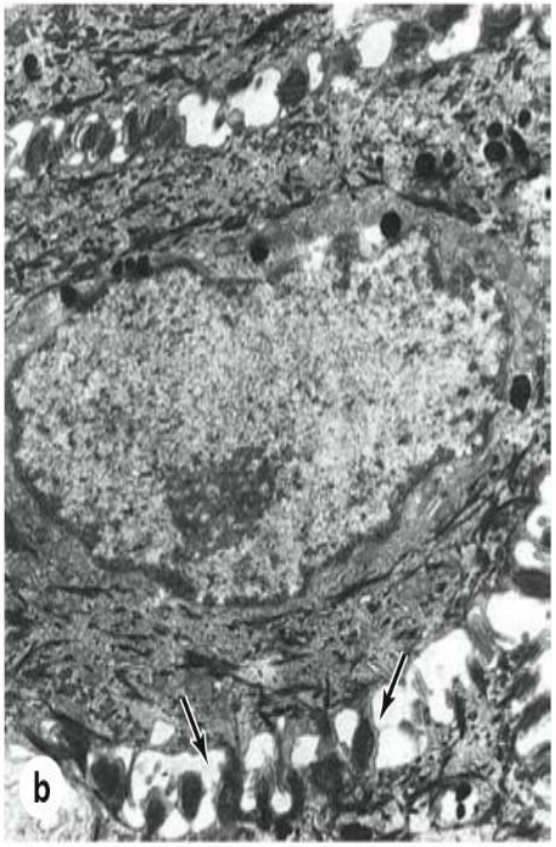
- From the dermis, the epidermis consists of **four** layers of keratinocytes (or **five** layers in thick skin, Figure 18–2):

■The **basal layer (stratum basale)** is a single layer of basophilic cuboidal or columnar cells on the basement membrane at the dermal-epidermal junction (Figures 18–2).

The **spinous layer (stratum spinosum)** is normally the thickest layer, especially in the epidermal ridges (Figures 18–2 and 18–3), and consists of generally polyhedral cells having central nuclei with nucleoli and cytoplasm actively synthesizing keratins.

FIGURE 18–4 Keratinocytes of the stratum spinosum.





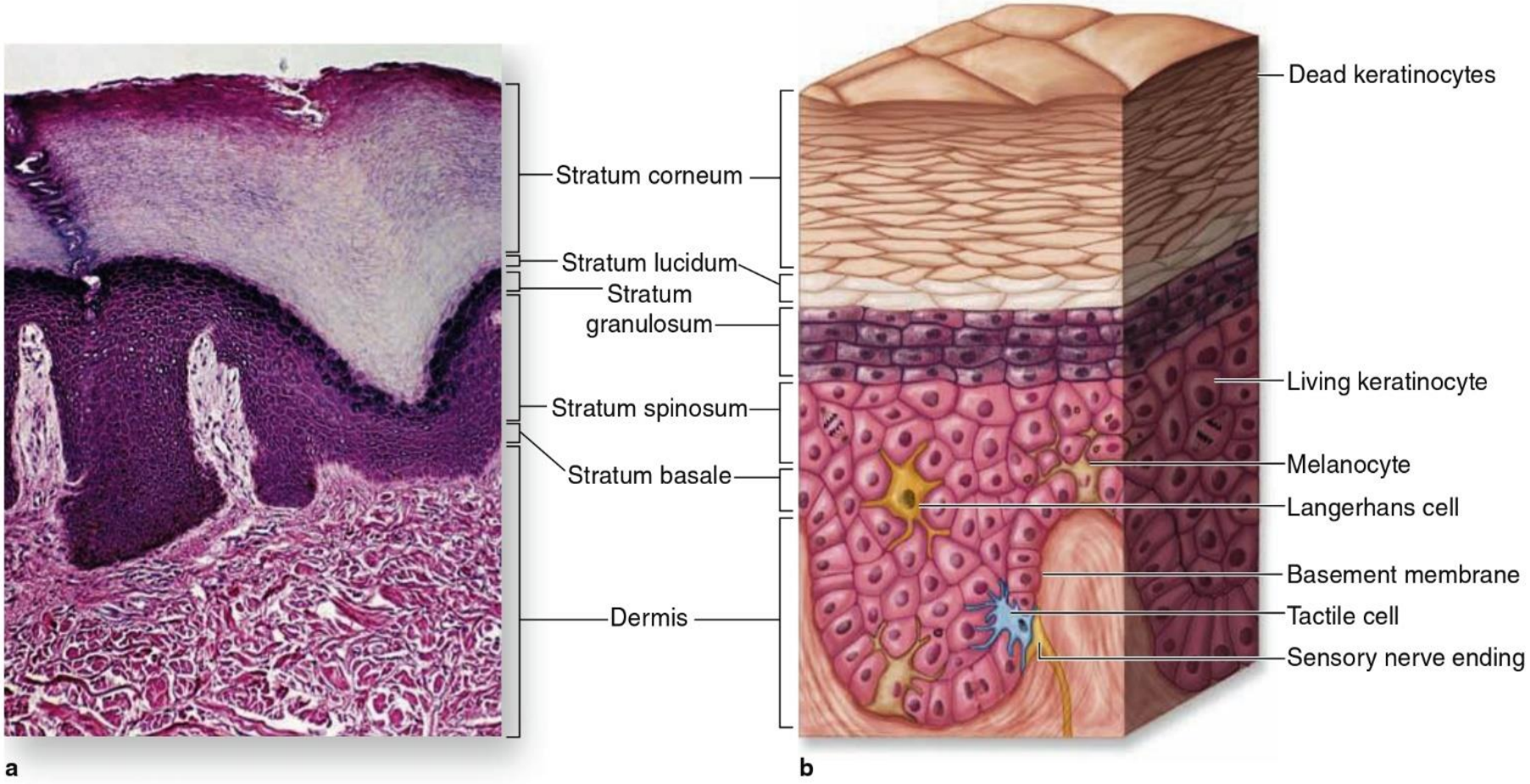
(a) A section of epidermal stratum spinosum of thick skin, showing cells with numerous short cytoplasmic projections (**arrow**). (X400; PT)

(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)

- The **granular layer (stratum granulosum)** consists of three to five layers of flattened cells, now undergoing the terminal differentiation process of **keratinization**. Their cytoplasm is filled with intensely basophilic masses (Figures 18–2 and 18–3; Figure 18–5) called **keratohyaline granules**.

Characteristic features in cells of the granular layer also include Golgi-derived **lamellar granules**, small ovoid structures (100 . 300 nm) with many lamellae containing various lipids and glycolipids.



(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)

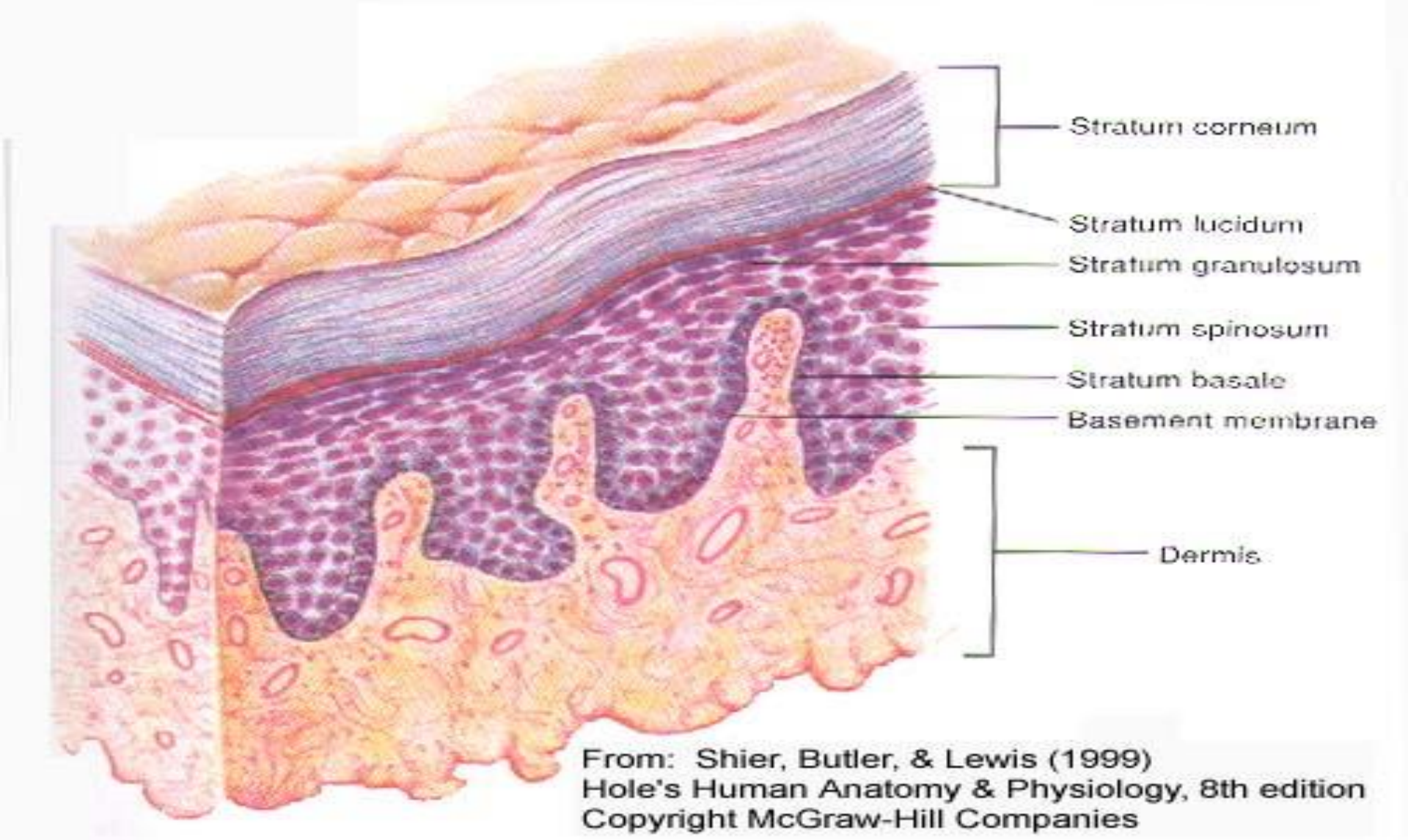
(b) Diagram illustrating the sequence of the epidermal layers also indicates the normal locations of three important nonkeratinocyte cells in the epidermis: melanocytes, a Langerhans cell, and a tactile Merkel cell.

Layers (strata) of epidermis in thick skin

- The stratum lucidum, found only in thick skin, consists of a thin, translucent layer of flattened eosinophilic keratinocytes held together by desmosomes (Figures 18–2 and 18–5). Nuclei and organelles have been lost, and the cytoplasm consists almost exclusively of packed keratin filaments embedded in an electron-dense matrix.

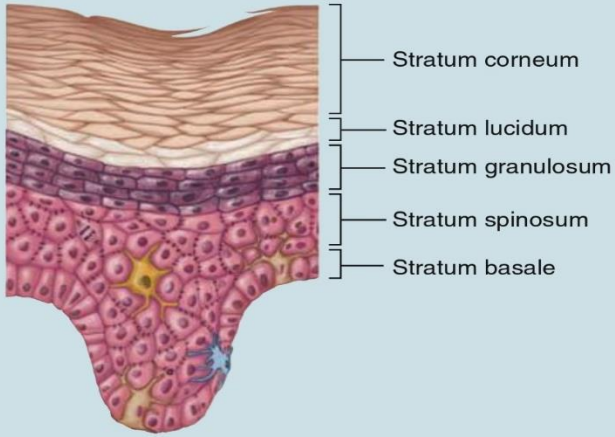
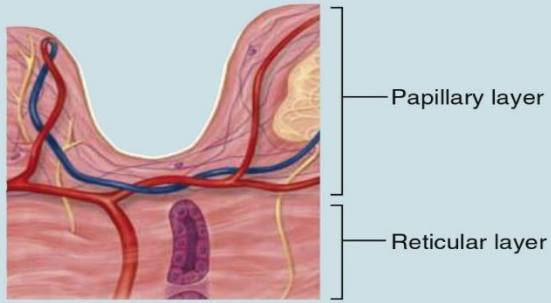
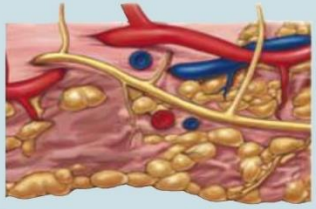
- The stratum corneum (Figures 18–2 and 18–3) consists of 15-20 layers of squamous, keratinized cells filled with birefringent filamentous keratins. Keratin filaments contain at least six different polypeptides with molecular

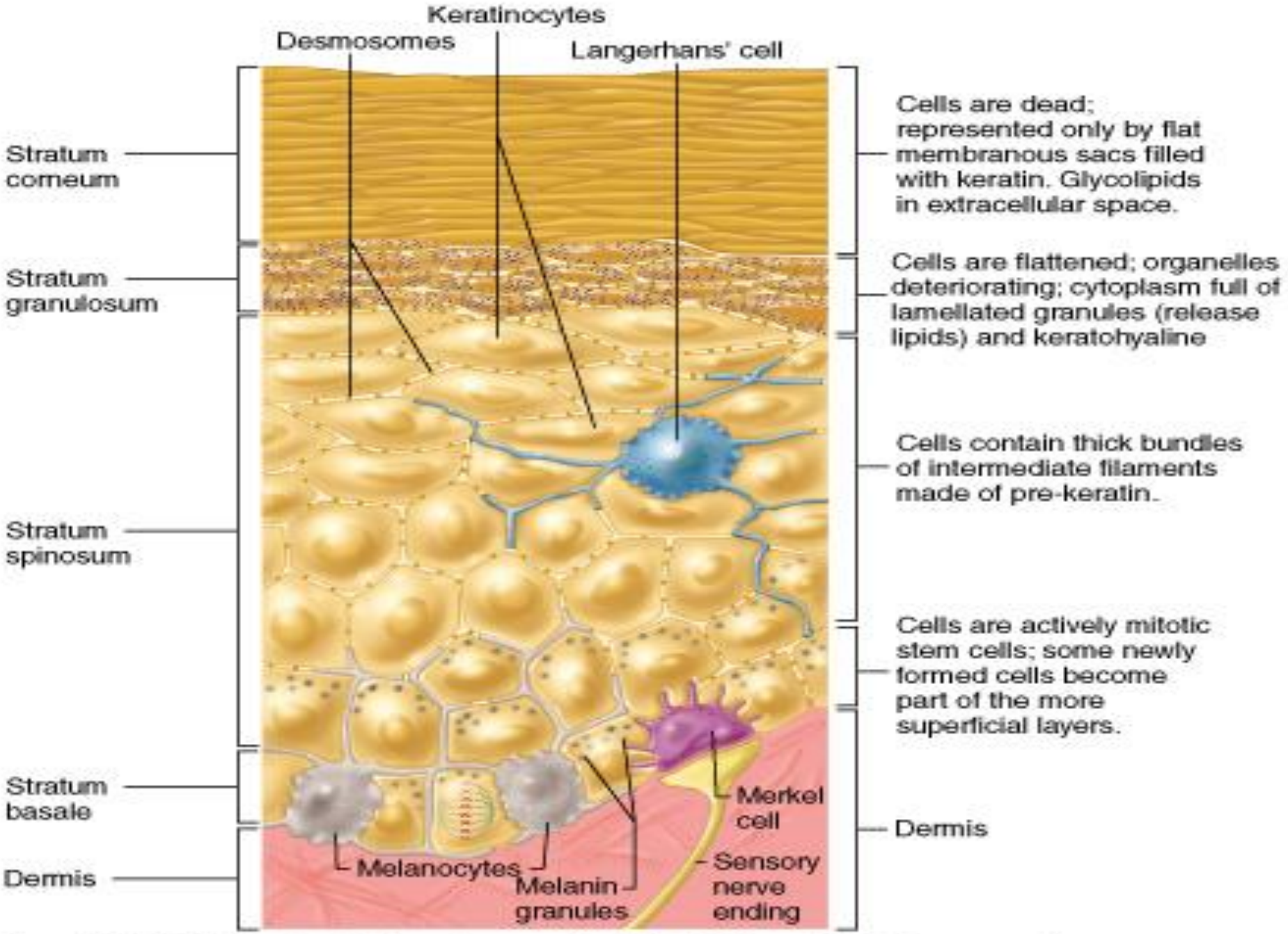
- Epidermis: keratinized stratified squamous epithelium with four distinct cell types and five distinct layers.



From: Shier, Butler, & Lewis (1999)
Hole's Human Anatomy & Physiology, 8th edition

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



Cells in the epidermis:

- keratinocytes
- melanocytes
- Merkel cells
- Langerhans' cells

1- **Keratinocytes**: most abundant

- produce keratin (fibrous protein)
- protective; water proofing the skin
- continuous mitosis
- form in the deepest layer called the stratum basal
- cells push their way up to the surface where they are dead cells filled with keratin.

Regenerates every 25-45 days.

- # Melanocytes

The color of the skin is the result of several factors, the most important of which are the keratinocytes' content of **melanin** and **carotene** and the number of blood vessels in the dermis.

Eumelanins are brown or black pigments produced by the **melanocyte**, a specialized cell of the epidermis found among the cells of the basal layer and in hair follicles.

Ultrastructurally a melanocyte has numerous small mitochondria, short cisternae of RER, and a well-developed Golgi apparatus.

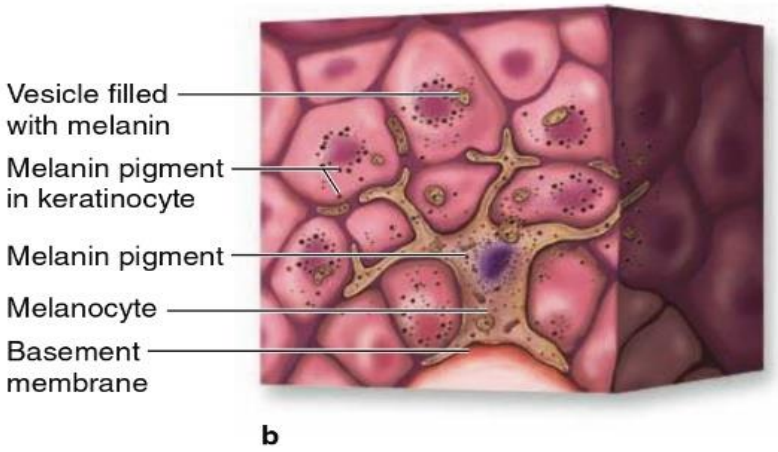
- # Melanocytes

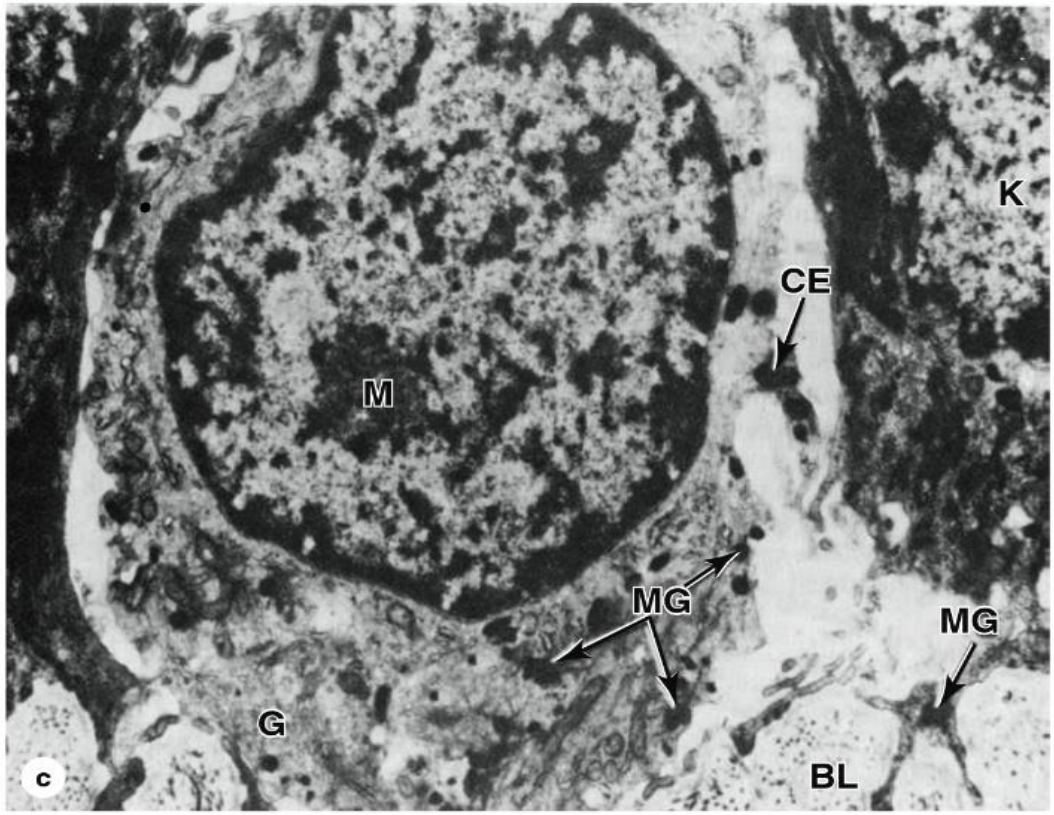
The first step in melanin synthesis is catalyzed by **tyrosinase**, a transmembrane enzyme in Golgi derived vesicles (Figure 18–7).

Tyrosinase activity converts tyrosine into **3,4-dihydroxyphenylalanine (DOPA)**, which is then further transformed and polymerized into the different forms of melanin.

Melanin pigment is linked to a matrix of structural proteins and accumulates in the vesicles until they form mature granules about 1-μm long called **melanosomes** (Figure 18–7).

FIGURE 18–6 Melanocytes.



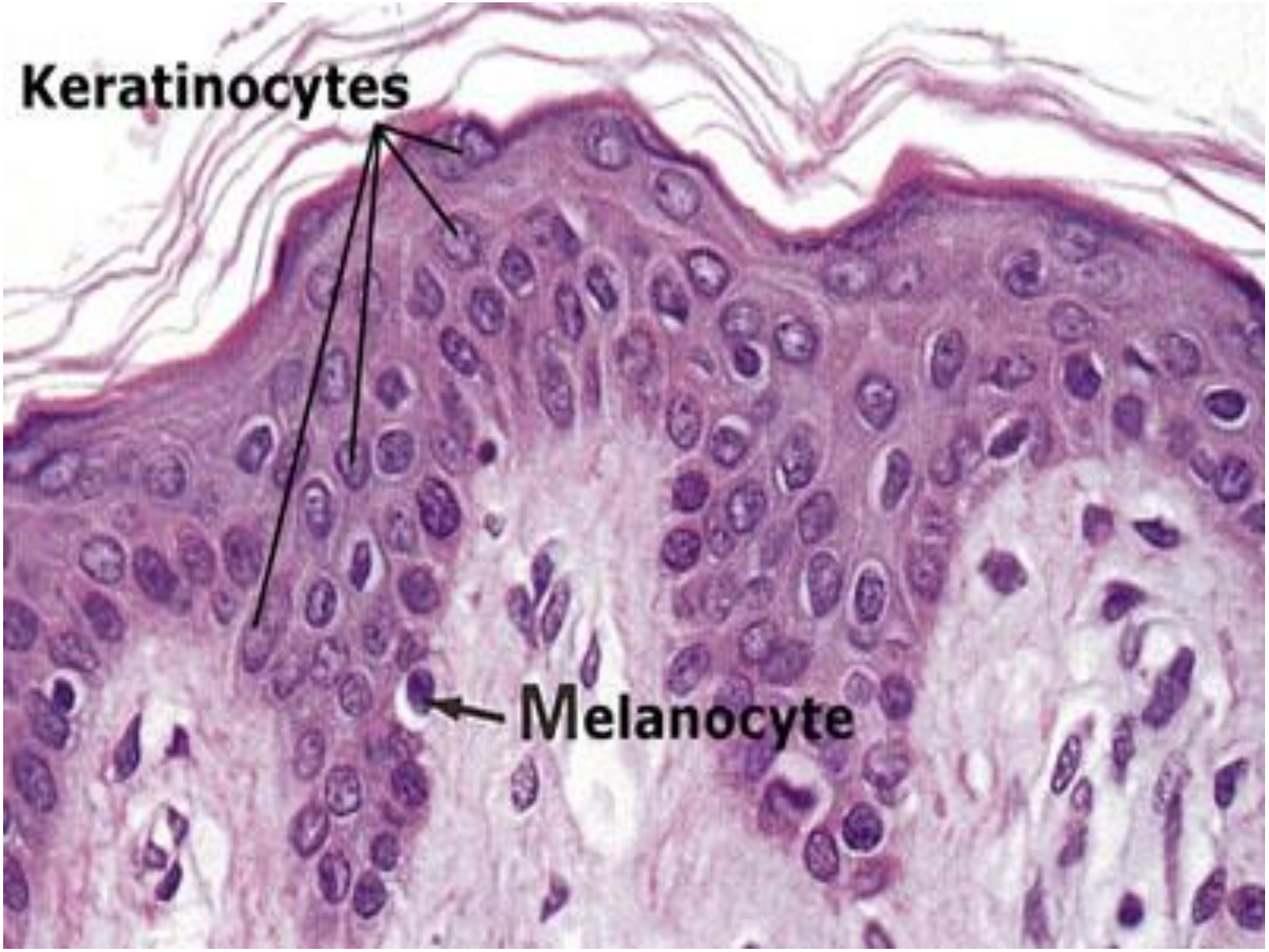


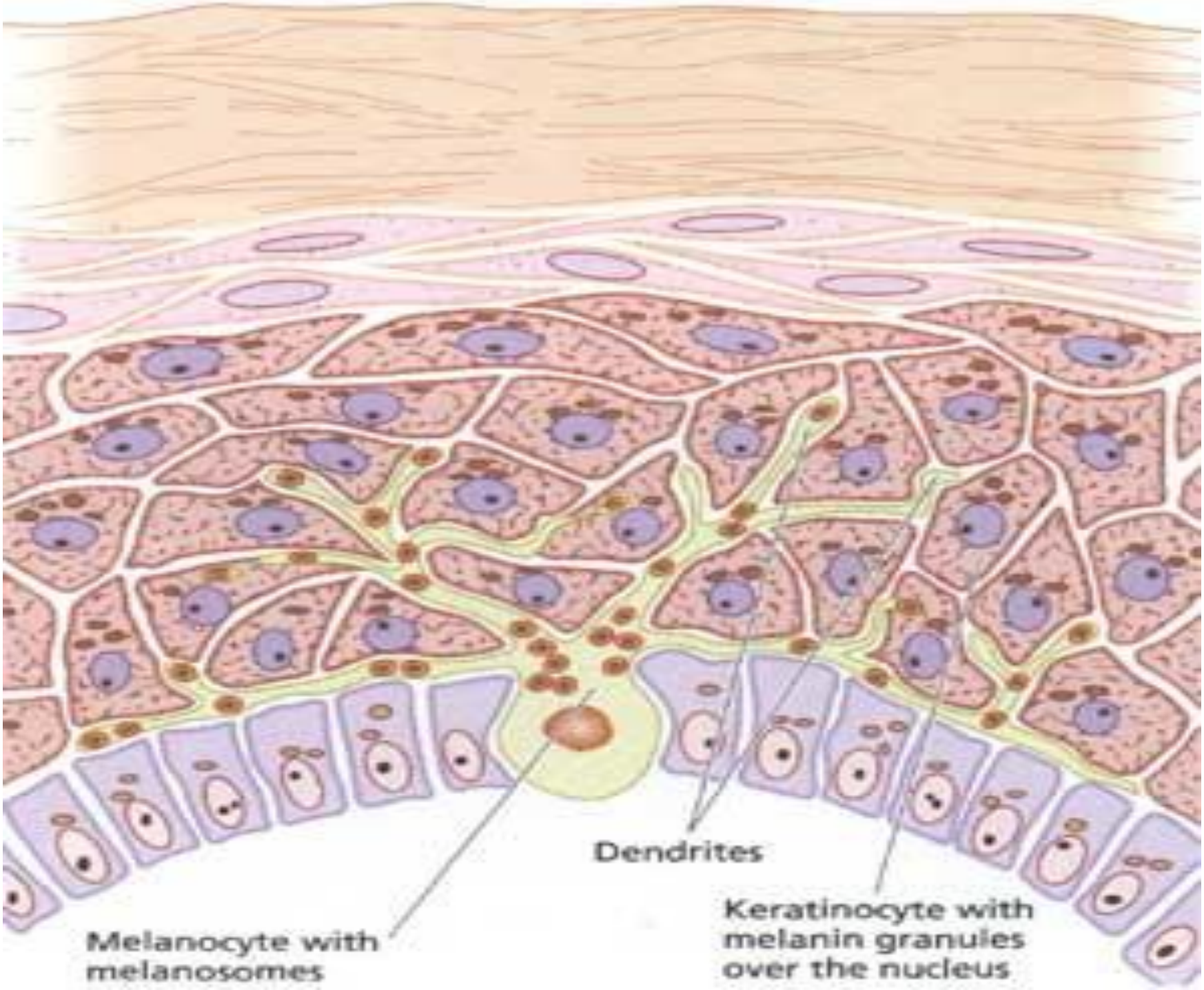
Melanocytes are located in the epidermal basal layer and synthesize **melanin granules** and transfer them into neighboring **keratinocytes**. Transfer occurs through many long, branching melanocyte processes that extend into the spinous layer and are not seen in routine microscopy.

(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)

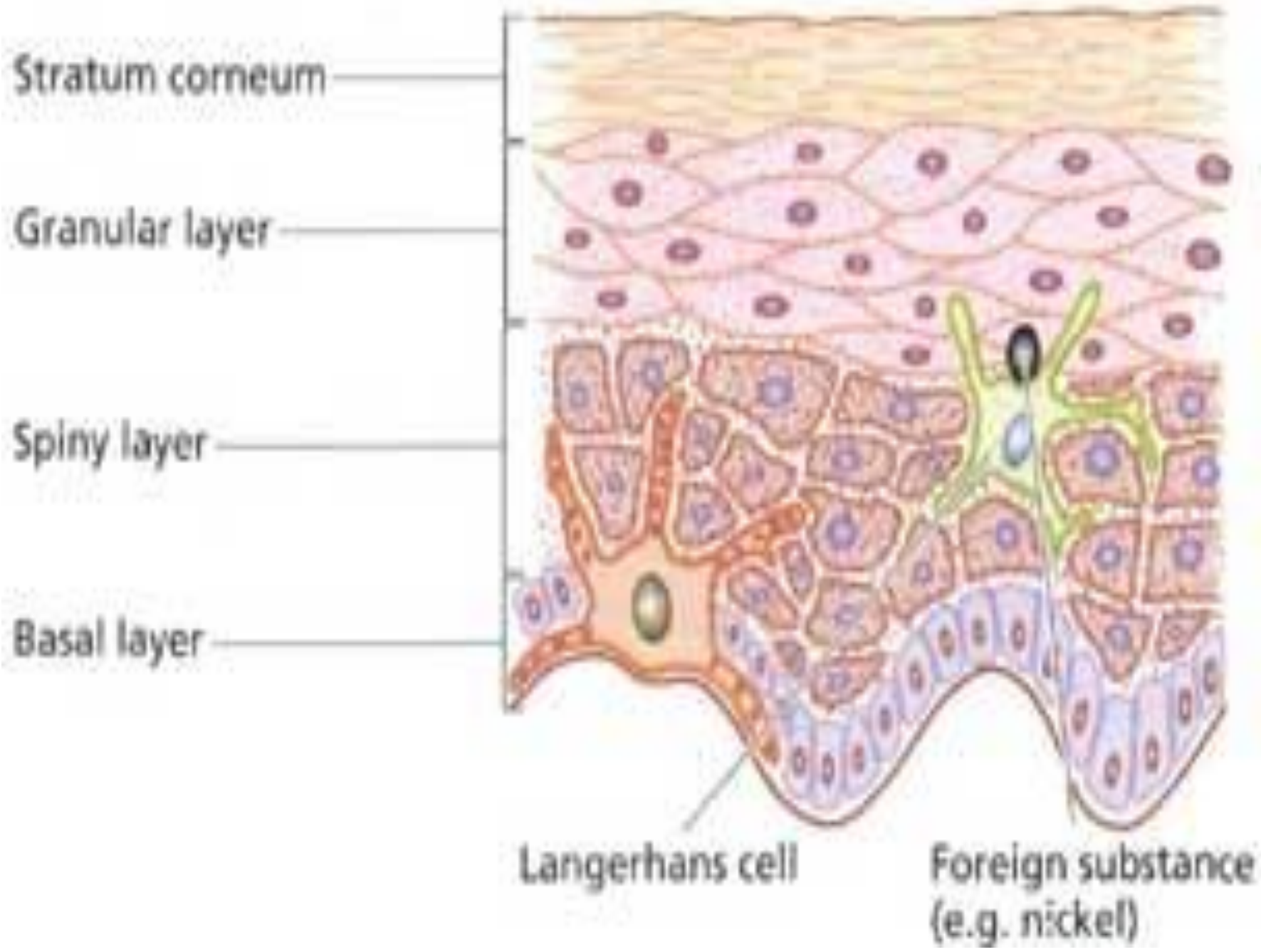

Keratinocytes
Melanocyte


Dendrites
Melanocyte with melanosomes
Keratinocyte with melanin granules over the nucleus

Langerhans Cells:

Antigen-presenting cells (APCs) called Langerhans cells, derived from monocytes, represent 2%-8% of the cells in epidermis and are usually most clearly seen in the spinous layer. Cytoplasmic processes extend from these dendritic cells between keratinocytes of all the layers, forming a fairly dense network in the epidermis (Figure 18–8).

- star-shaped cells arising from bone marrow that migrate to epidermis.
- epidermal dendritic cells (macrophages)
- interact with a WBC called a T- helper cell
- easily damaged by UV light.

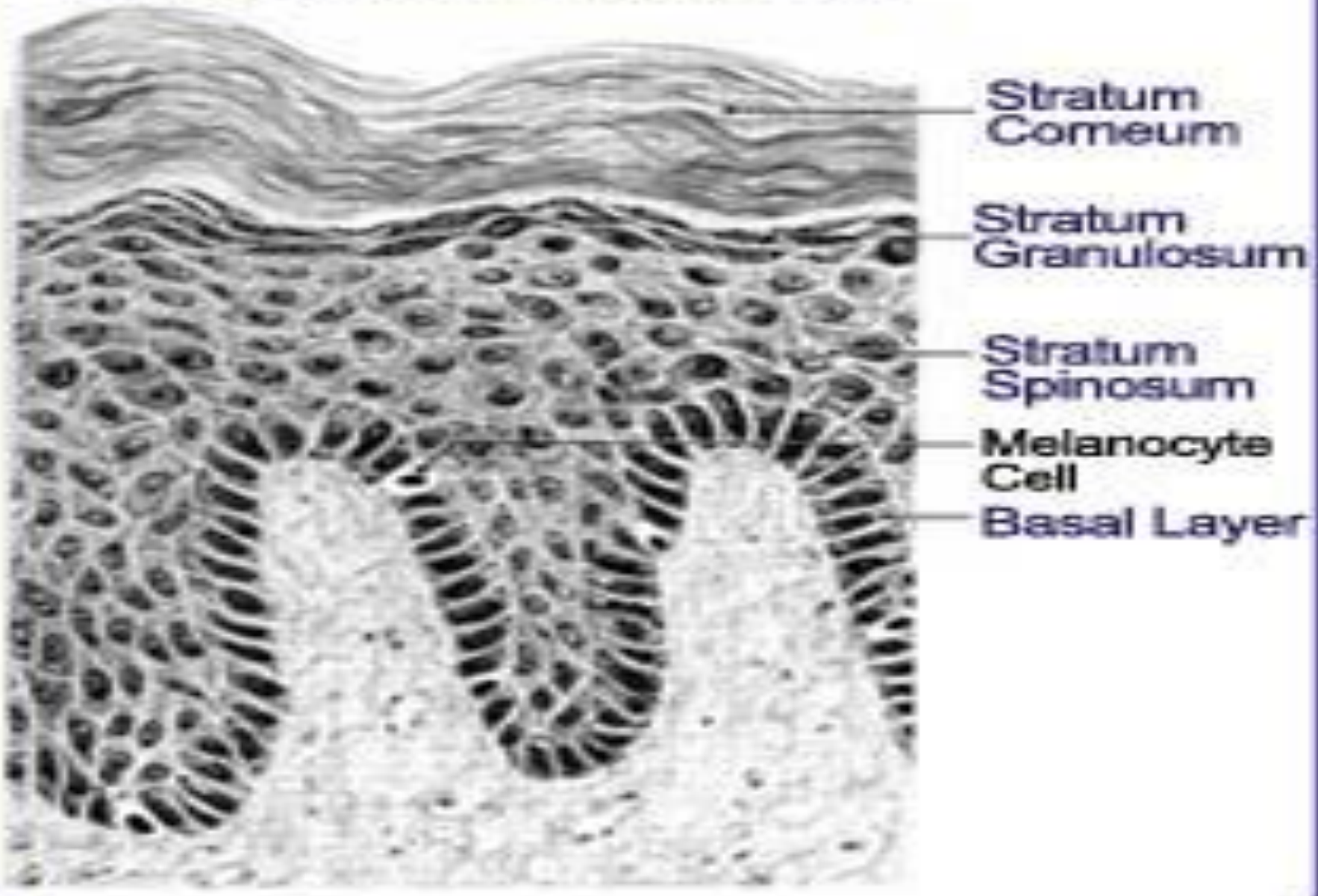

Stratum corneum
Granular layer
Spiny layer
Basal layer
Langerhans cell
Foreign substance
(e.g. nickel)

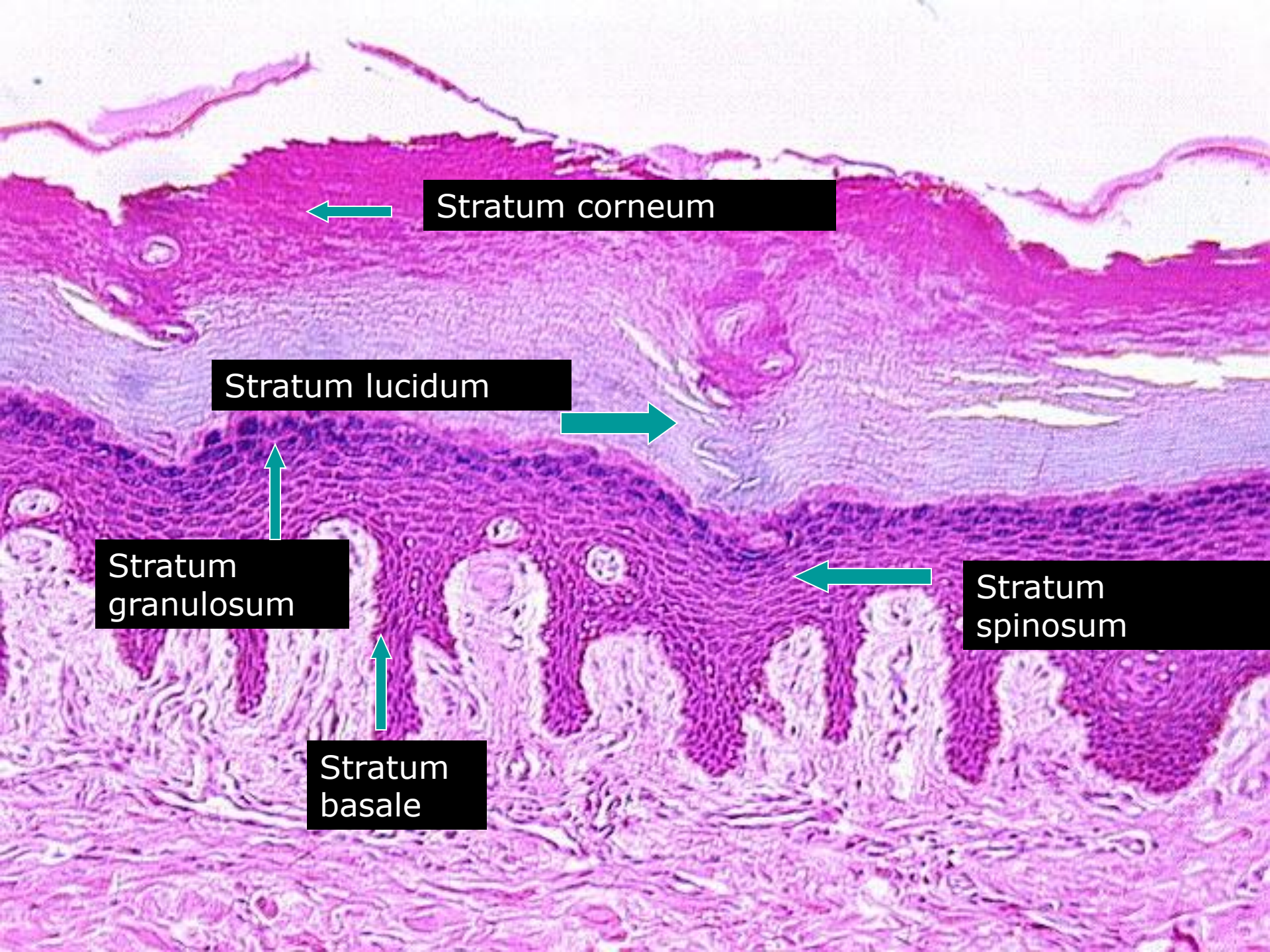
Merkel Cells

Merkel cells, or **epithelial tactile cells**, are sensitive mechanoreceptors essential for light touch sensation. Joined by desmosomes to keratinocytes of the basal epidermal layer,
Merkel cells resemble the surrounding cells but with few, if any, melanosomes.

They are abundant in highly sensitive skin like that of Fingertips and at the bases of some hair follicles. Merkel cells originate from the same stem cells as keratinocytes and are characterized by small, Golgi-derived dense-core neurosecretory granules containing peptides (Figure 18–9).

Layers of the Epidermis




Stratum corneum
Stratum lucidum
Stratum granulosum
Stratum spinosum
Stratum basale

5 layers of the epidermis:

1- Stratum corneum (horny layer)

- layer has many rows of dead cells filled with keratin
- effective barrier against light, heat and bacteria
- 20-30 cell layers thick

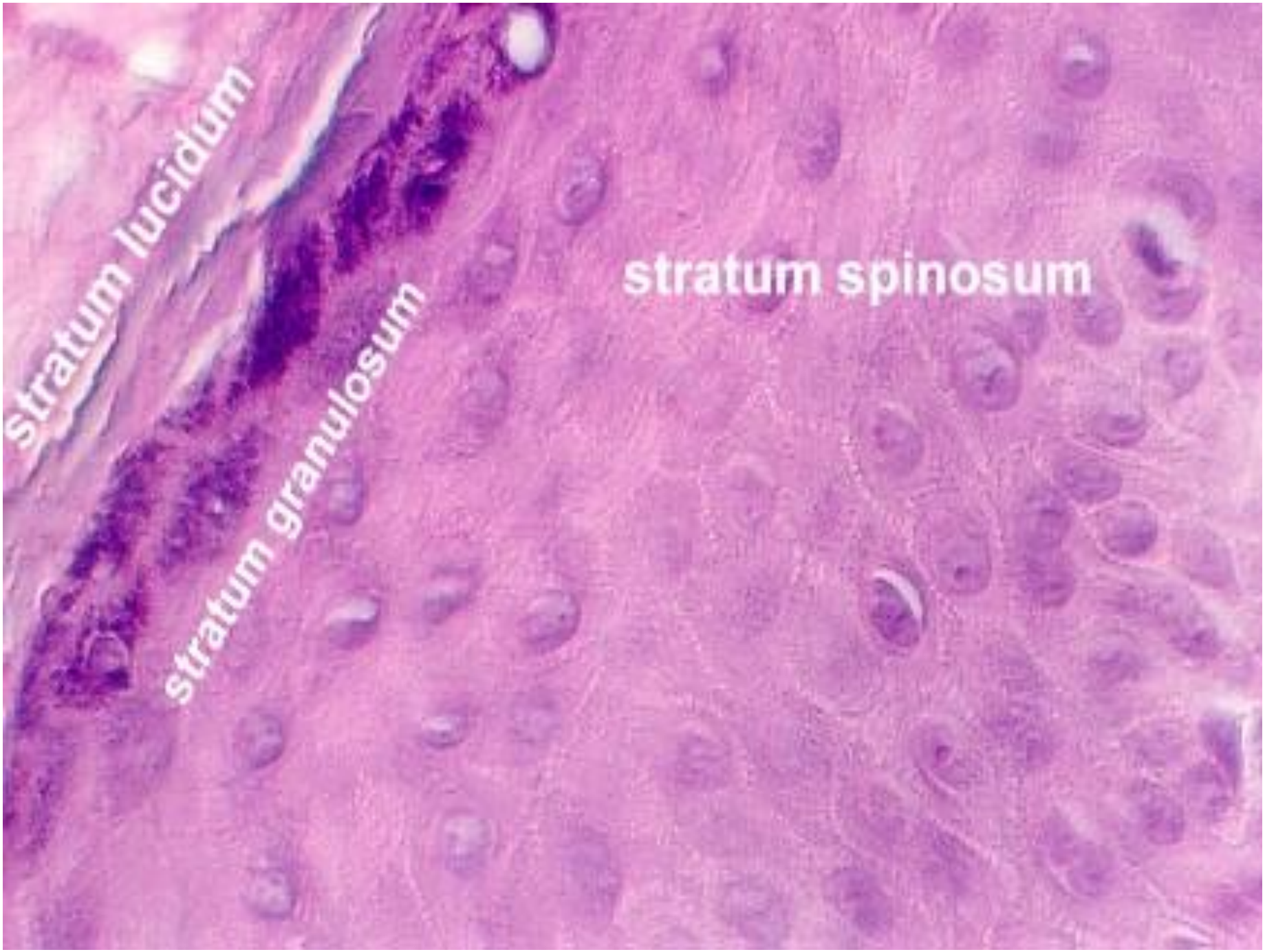
2- Stratum lucidum

- seen in thick skin of the palms and soles of feet.
  - 3-5 rows of clear flat dead cells

3- Stratum granulosum

- 3-5 rows of flattened cells
- nuclei of cells flatten out
- keratohyalin granules (darkly stained) accumulate
- lamellated granules secrete glycolipids into extracellular spaces to slow water loss in the epidermis

4- Stratum spinosum: “spiny layer”
- 8-10 rows of polyhedral (many sided) cells
- appearance of prickly spines
- melanin granules and Langerhans’ cell predominate


Stratum lucidum
stratum granulosum
stratum spinosum

5- Stratum basal: deepest epidermal layer

- attached to dermis
- single row of cells
- mostly columnar keratinocytes
- with rapid mitotic division
- stratum germinativum
- contain merkel cells and melanocytes
- 10-25%

- Dermis:
  - flexible and strong connective tissue
  - elastic, reticular and collagen fibers
  - cells: fibroblasts, macrophages (WBC), mast cells (histamine).
  - nerves, blood and lymphatic vessels
  - oil and sweat glands originate
  - two layers: papillary and reticular

The dermis is the layer of connective tissue (Figures 18–1 and 18–2) that supports the epidermis and binds it to the subcutaneous tissue (hypodermis).

The thickness of the dermis varies with the region of the body and reaches its maximum of 4mm on the back.

The surface of the dermis is very irregular and has many projections (dermal papillae) that interdigitate with projections (epidermal pegs or ridges) of the epidermis (Figure 18–1), especially in skin subject to frequent pressure, where they reinforce the dermal-epidermal junction.

A **basement membrane** always occurs between the stratum basale and the dermis, and follows the contour of the interdigitations between these layers.

Nutrients for keratinocytes diffuse into the avascular epidermis from the dermal vasculature through the basement membrane.

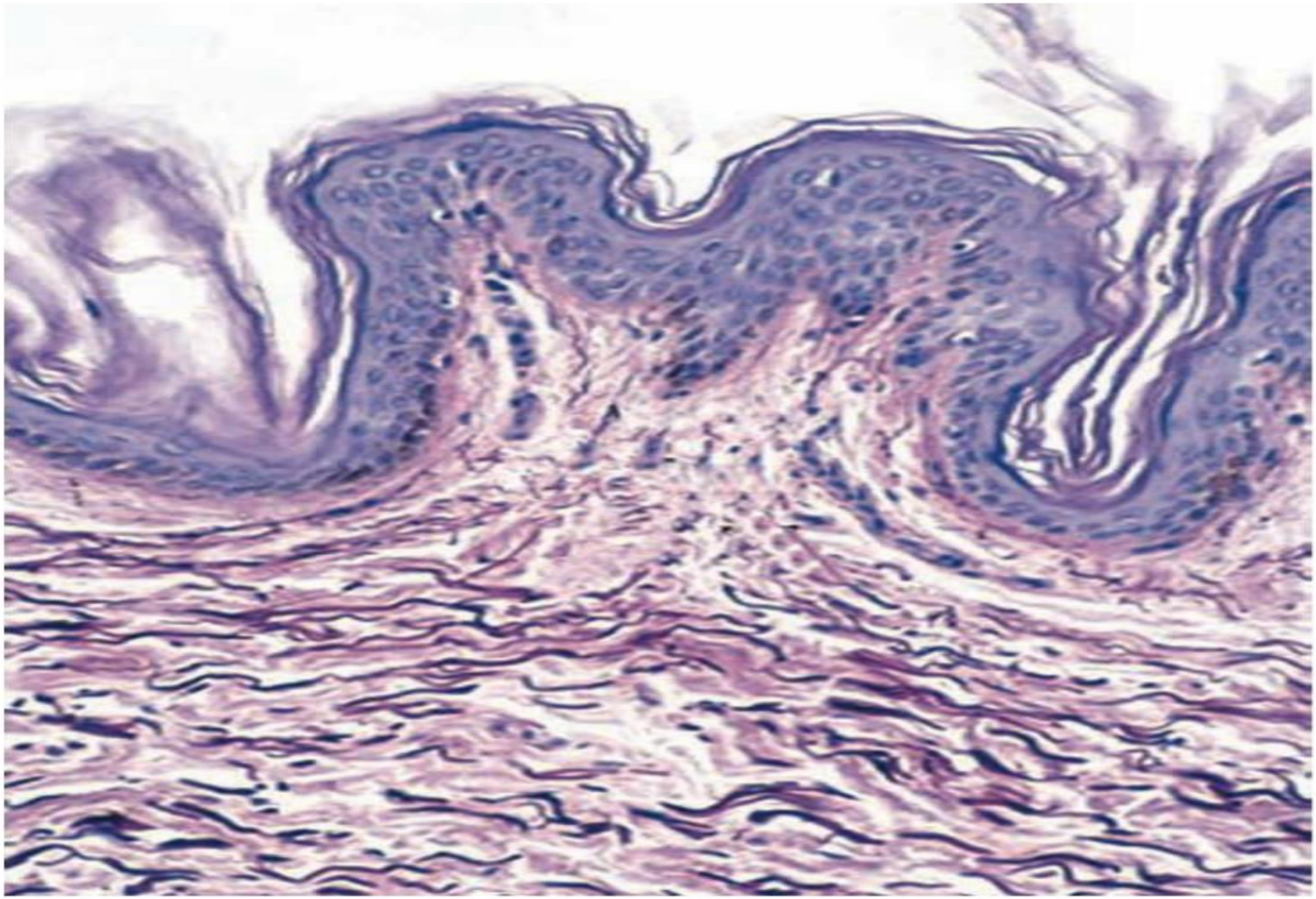
The dermis contains two sublayers with indistinct boundaries (Figure 18–1; Table 18–1):

- The thin **papillary layer**, which includes the dermal papillae, consists of loose connective tissue, with types I and III collagen fibers, fibroblasts and scattered mast cells, dendritic cells, and leukocytes. From this layer, anchoring fibrils of type VII collagen insert into the basal lamina, helping to bind the dermis to the epidermis.

■ The underlying reticular layer is much thicker, consists of dense irregular connective tissue (mainly bundles of type I collagen), with more fibers and fewer cells than the papillary layer.

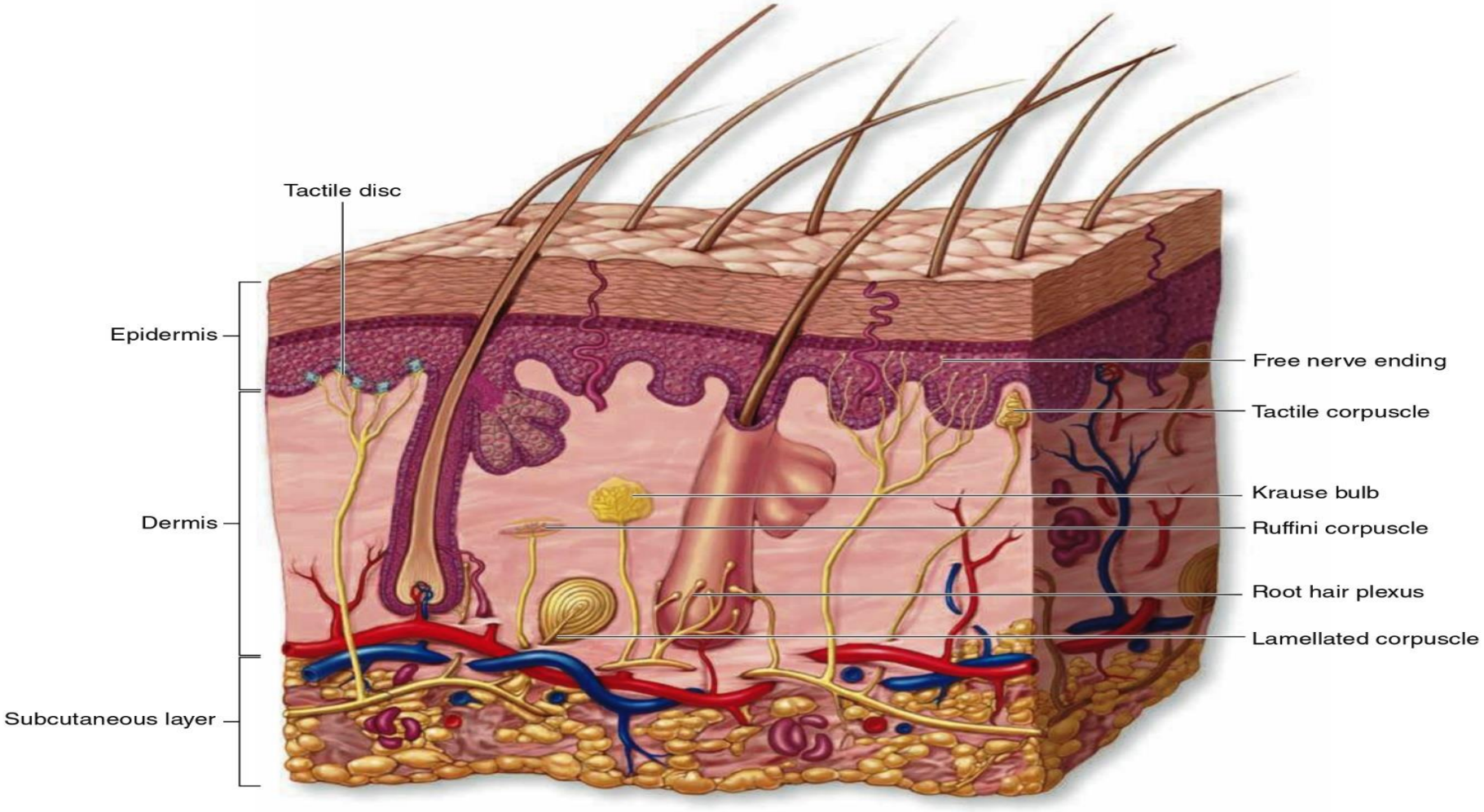
A network of elastic fibers is also present (Figure 18–10), providing elasticity to the skin. Between the collagen and elastic fibers are abundant proteoglycans rich in dermatan sulfate.

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)

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 low-frequency vibrations/movements, and **Ruffini corpuscles** detecting tissue distortion. The latter two receptors are less widely distributed in skin and less commonly seen.

- 1- Papillary layer:
- - loose connective tissue with nipple like surface projection called dermal papilla.
- - capillaries
- - contain pain receptors
- - contain touch receptors (Meissner's corpuscles
- - dermal ridges- epidermal ridges- pattern called fingerprints

- 2- Reticular layer:
  - dense irregular c.t.
  - collagen fibers offer strength
  - holds water
  - dermal tearing causes stretch marks.

Skin color: attributed to melanin, hemoglobin and carotene.

- Hair histology:

- composed of dead columns of keratinized cells.

- shaft: is the superficial portion of hair

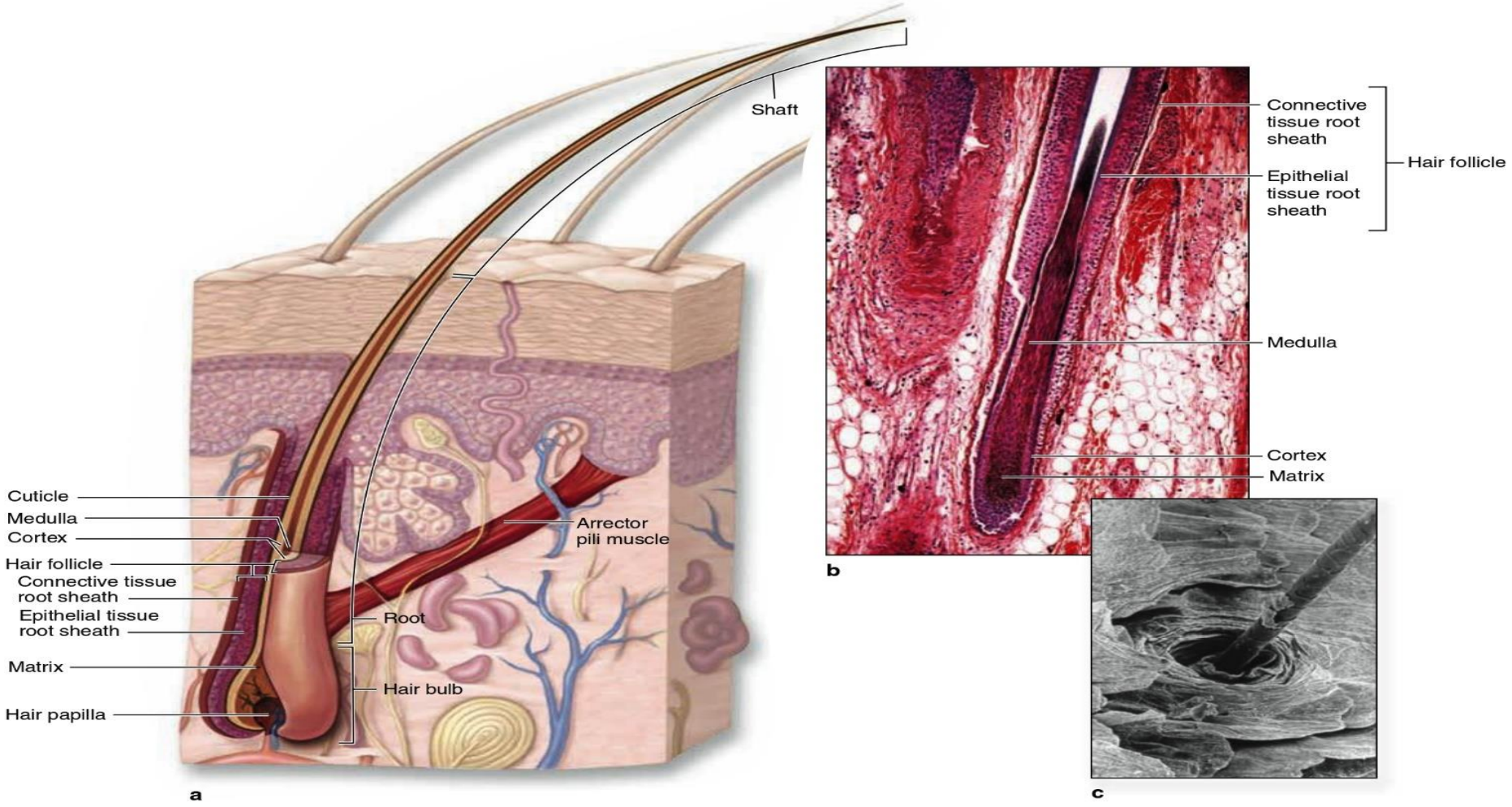
- root: below the surface in the dermis.

Shaft and root are composed of three layers: inner medulla, middle cortex and outer cuticle.

Inner medulla has 2-3 rows of polyhedral cells where pigment is located

Cortex is major portion of shaft

FIGURE 18–13 Hair.



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)

Hair follicle surrounds the root.

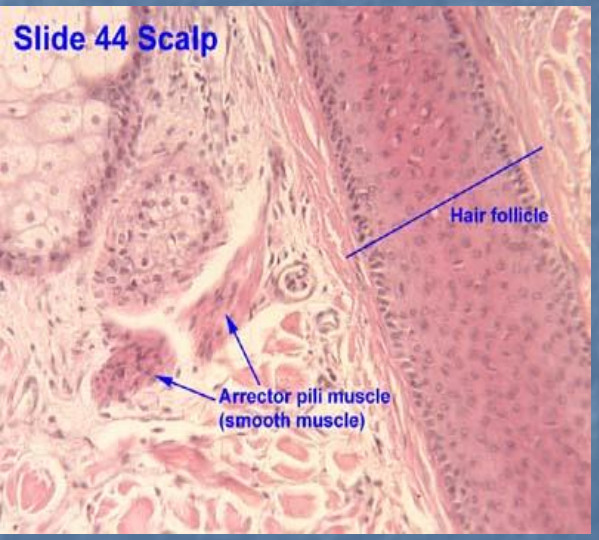
Bulb is the enlargement at the end of the follicle.

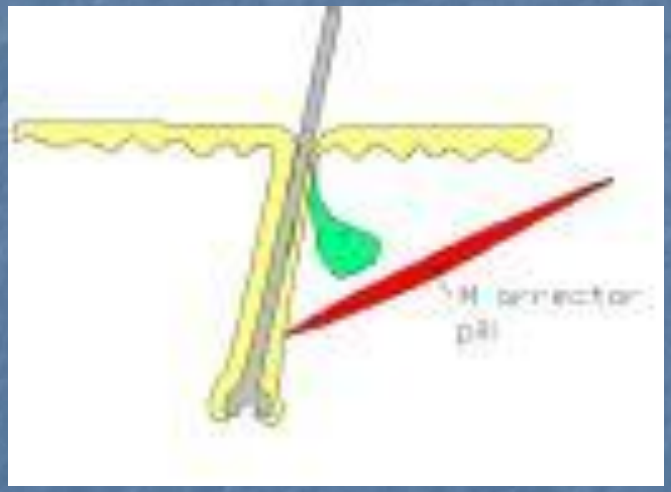
- Also houses the germinal layer

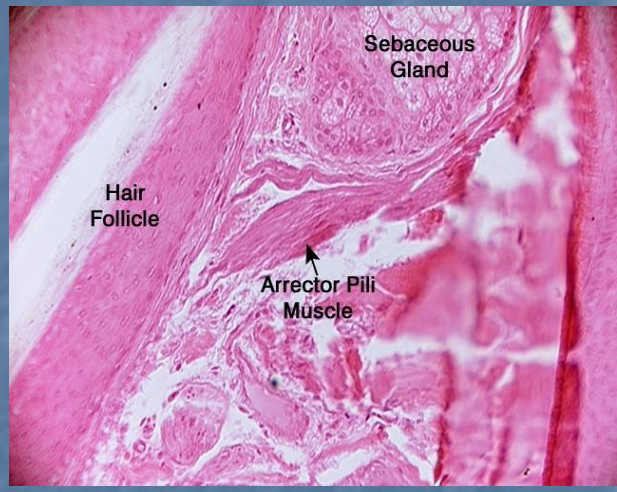
Papilla (nipple like) is located in the bulb and is where the blood supply nourishes the hair.

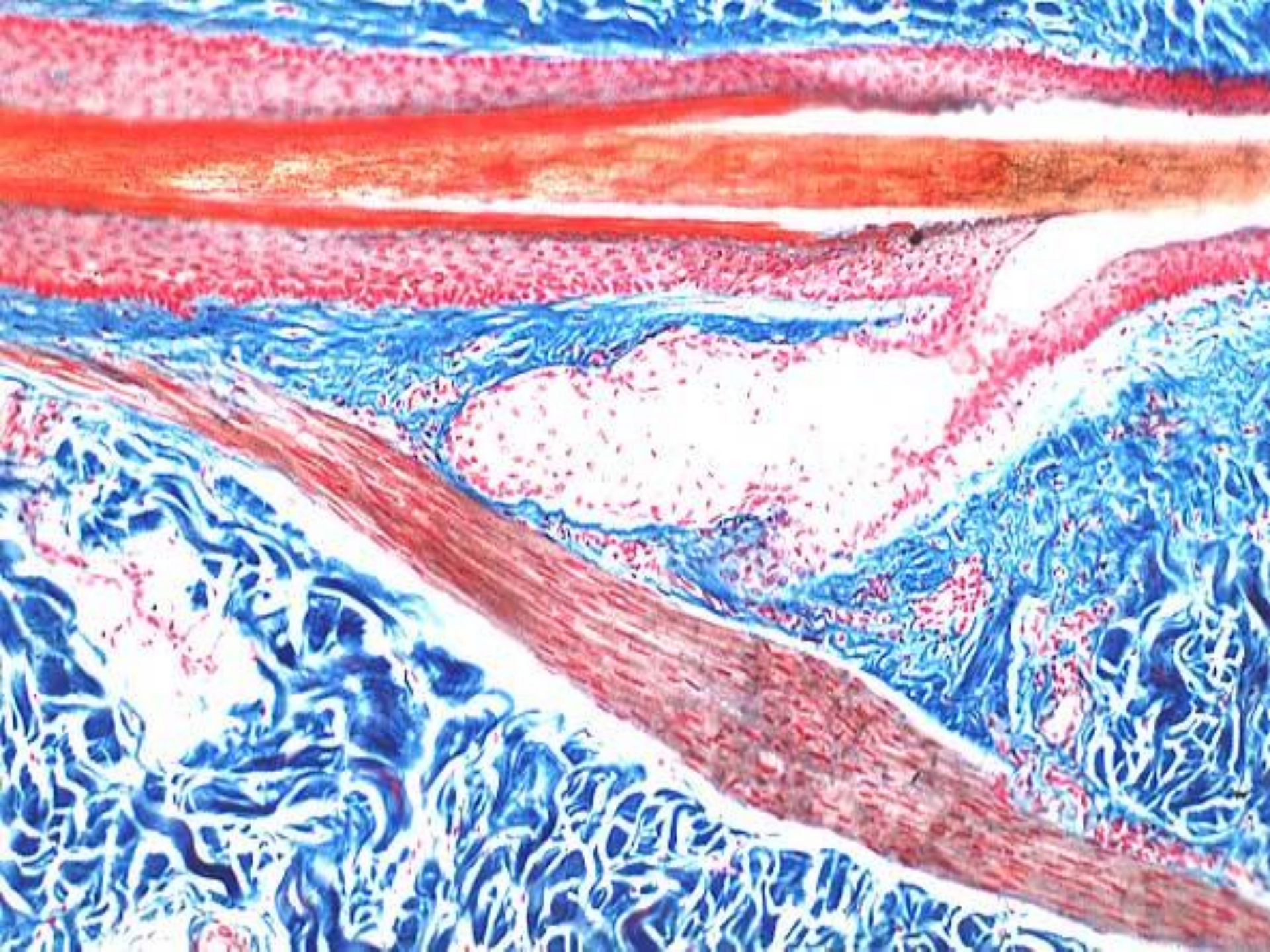
Arrector pili (pl. pilorum) is smooth muscle located in the dermis and is attached to the side of the hair shaft.

- fright, cold and emotions will contract muscle and pull hair in vertical position. “Goose bumps”.









Glands:

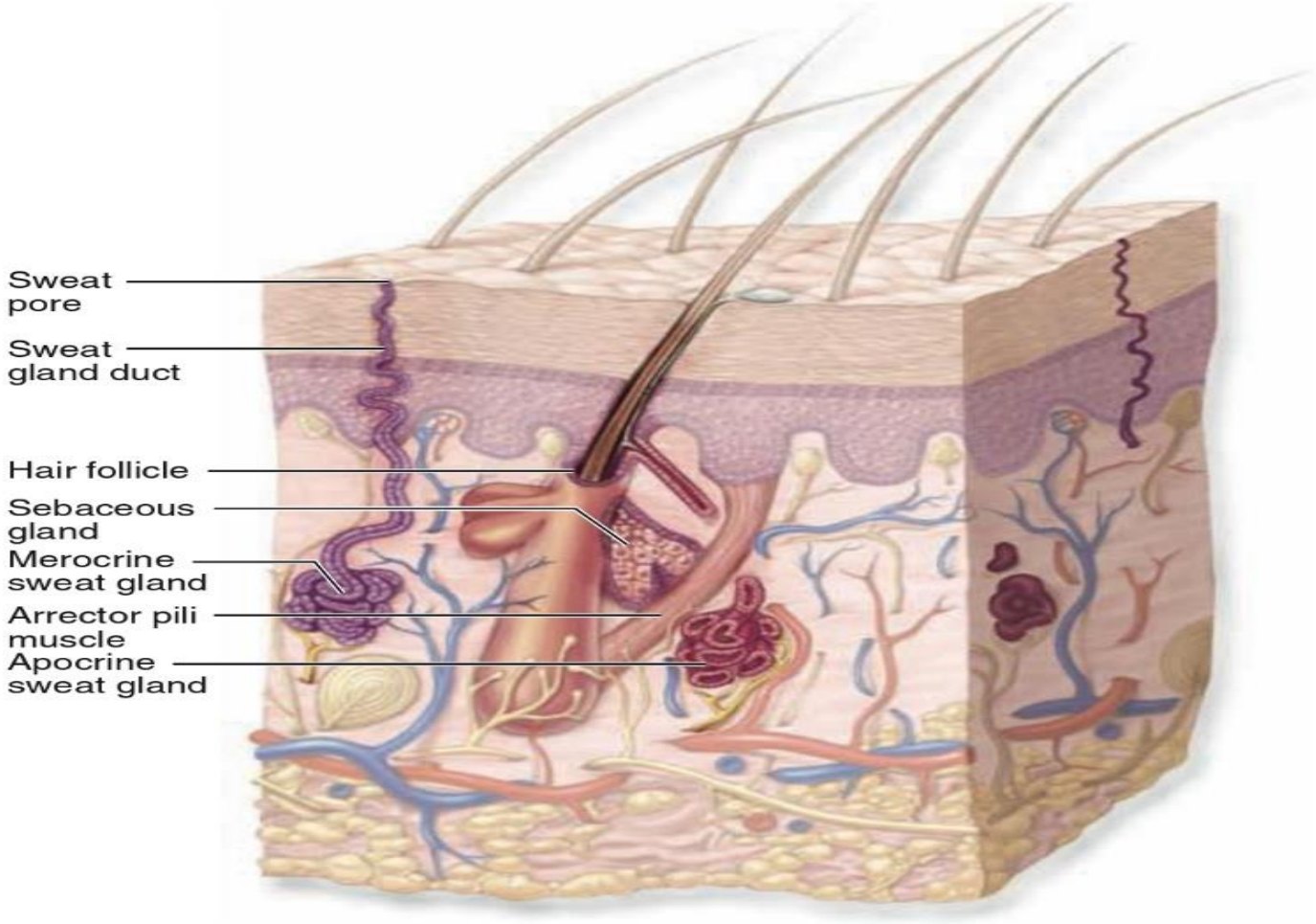
Two types of glands exist in the integument.

- Sebaceous glands (oil glands)
- Sweat glands

Sebaceous glands: (holocrine glands)

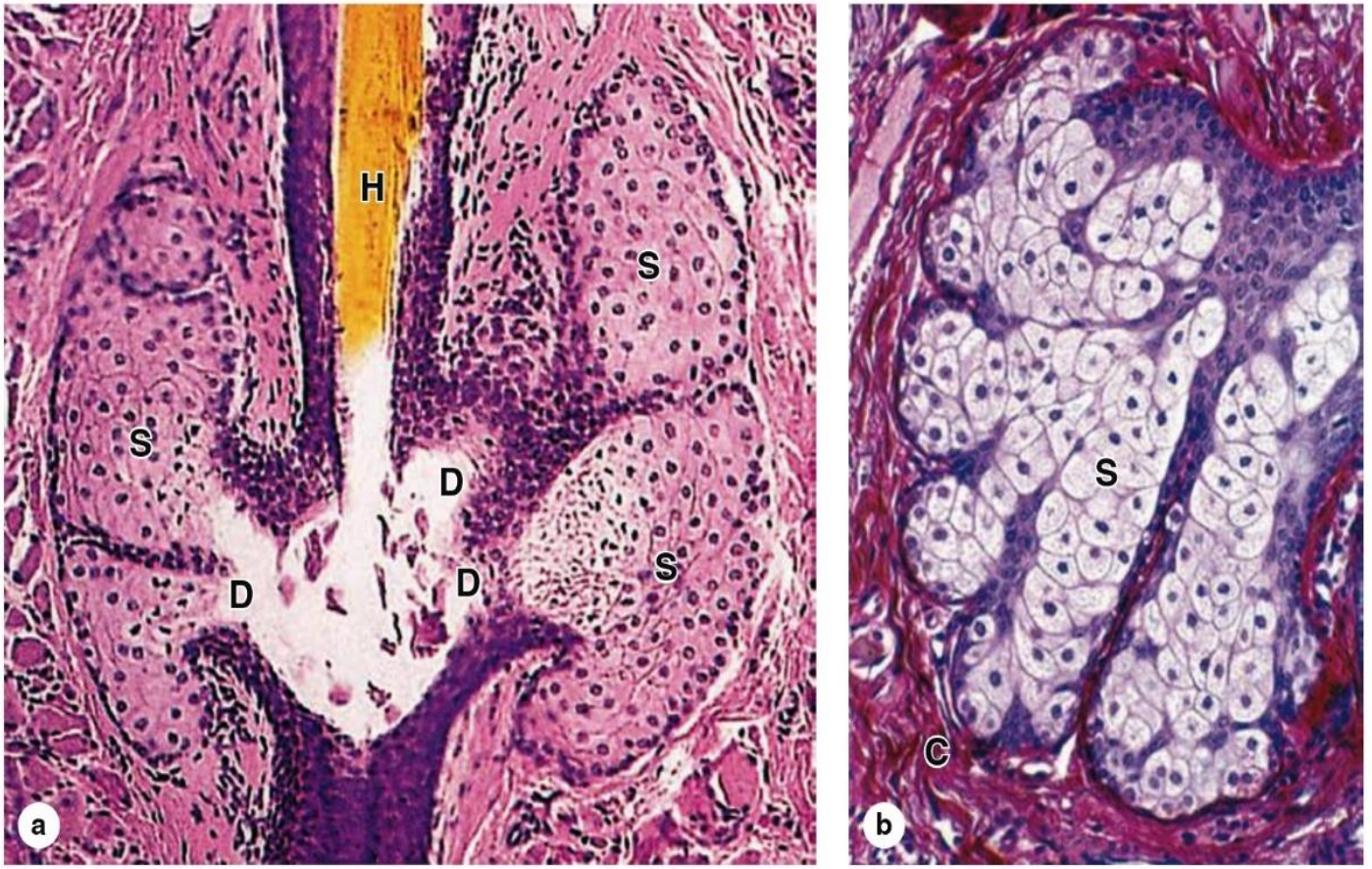
- connected to hair follicle
- not found on palms and soles of feet
- secretes sebum (fats, cholesterol and proteins
- keep hair from drying out, keeps skin moist
- whiteheads, blackheads and acne

FIGURE 18–16 Glands of skin.



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.

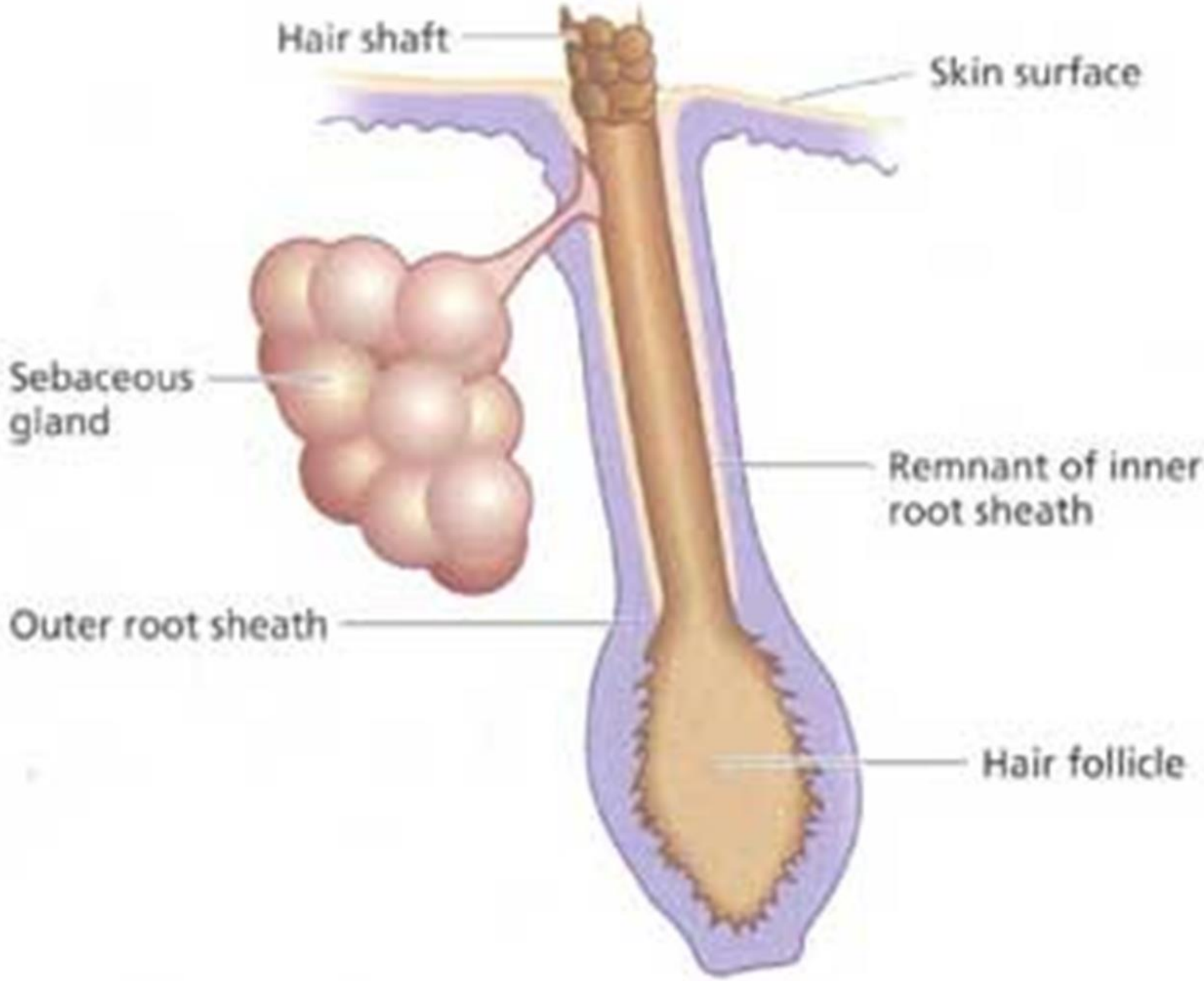
FIGURE 18–17 Sebaceous glands.

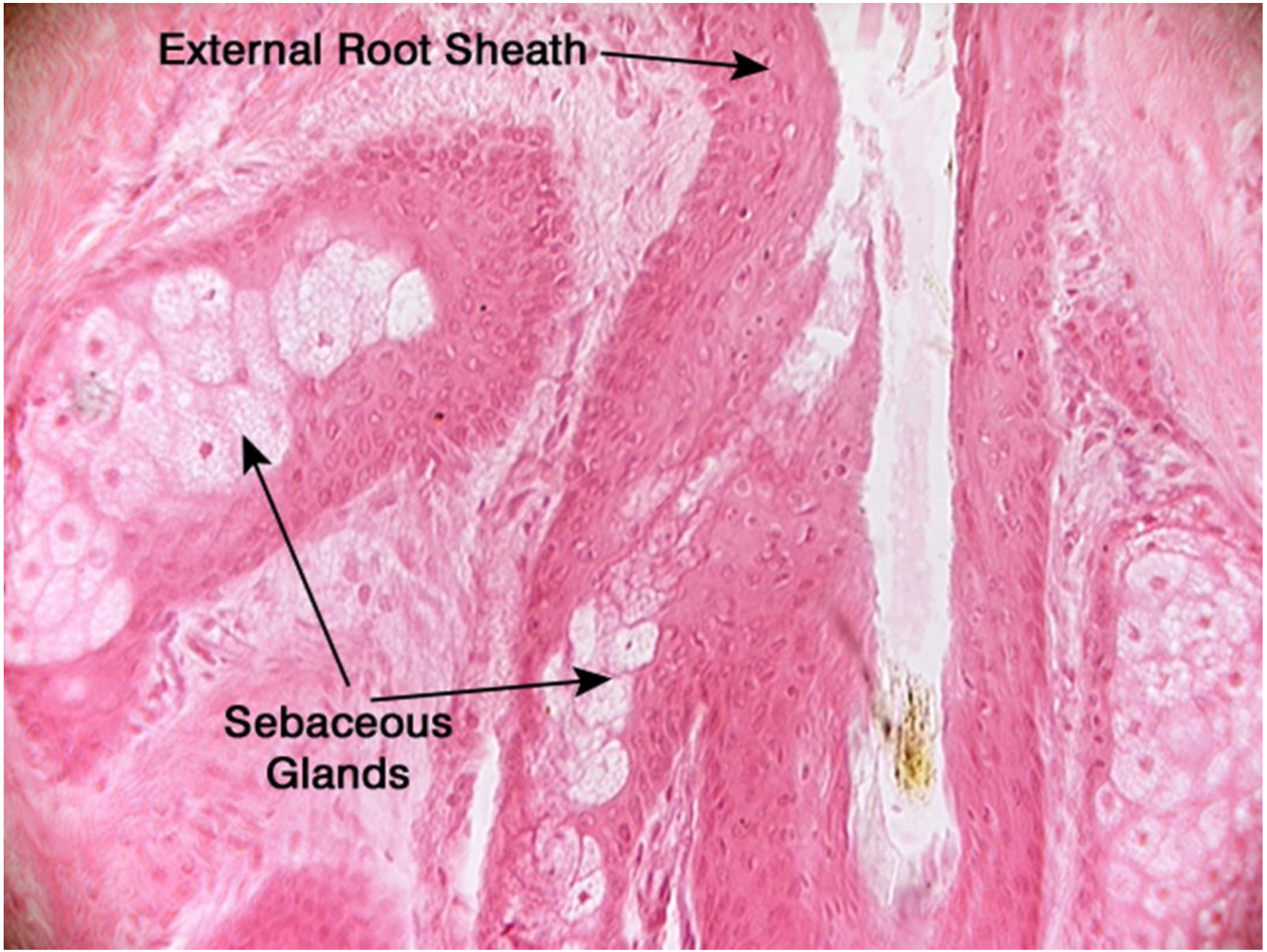


Sebaceous glands secrete a complex, oily mixture of lipids called **sebum** into short ducts that in most areas open into hair follicles. Sebum production is the classic example of holocrine secretion, in which the entire cell dies and contributes to the secretory product.

(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)

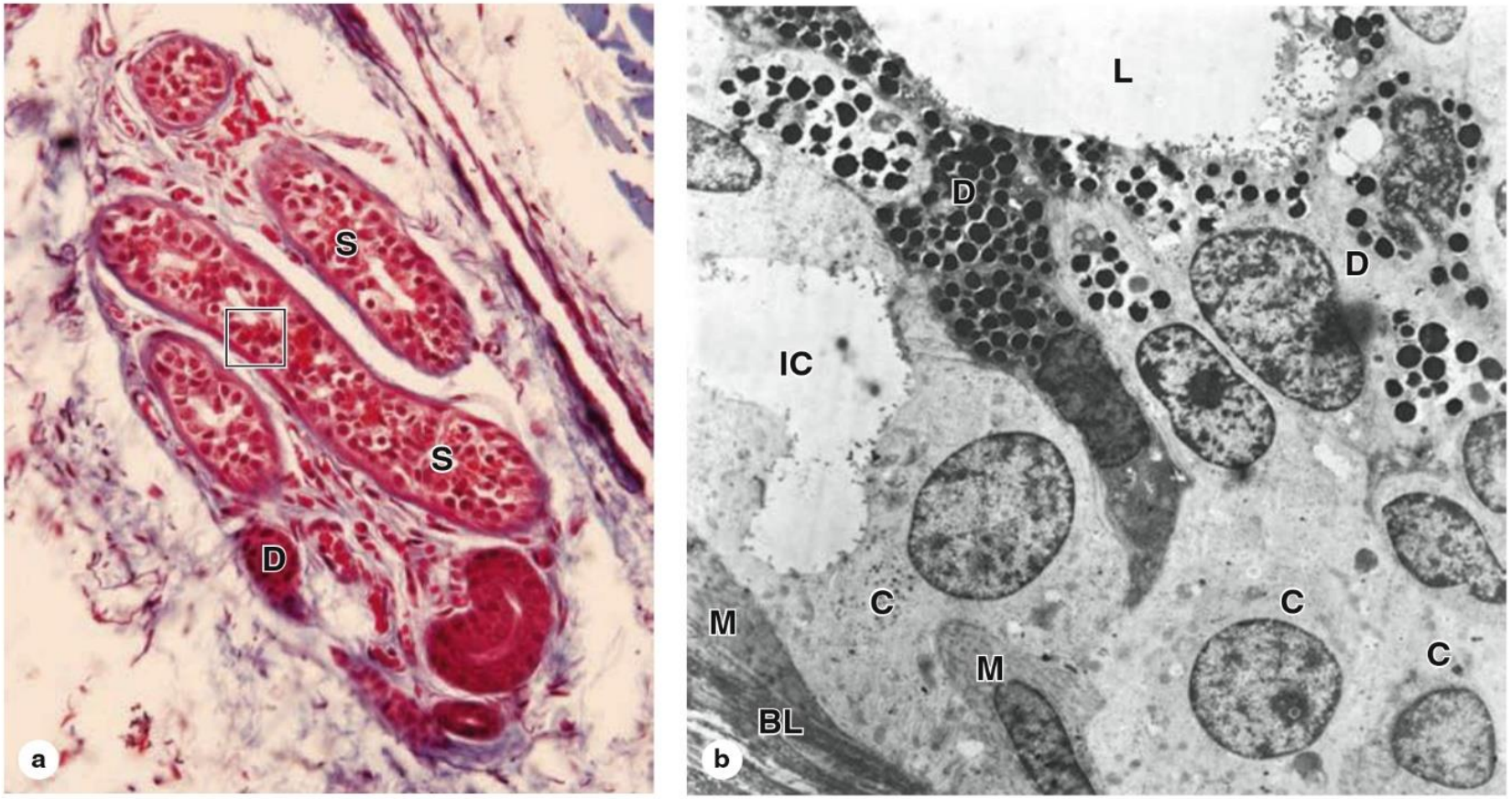

Hair shaft
Skin surface
Sebaceous gland
Remnant of inner root sheath
Outer root sheath
Hair follicle


External Root Sheath
Sebaceous
Glands

Sweat glands: exocrine glands

- millions located throughout the skin
- two types:
  - eccrine: more common (merocrine)
    - originate in subQ layer
    - palms and soles of feet
    - sweat is watery (99% H_20)
    - sweating regulated by sympathetic nervous system

FIGURE 18–18 Eccrine sweat glands.



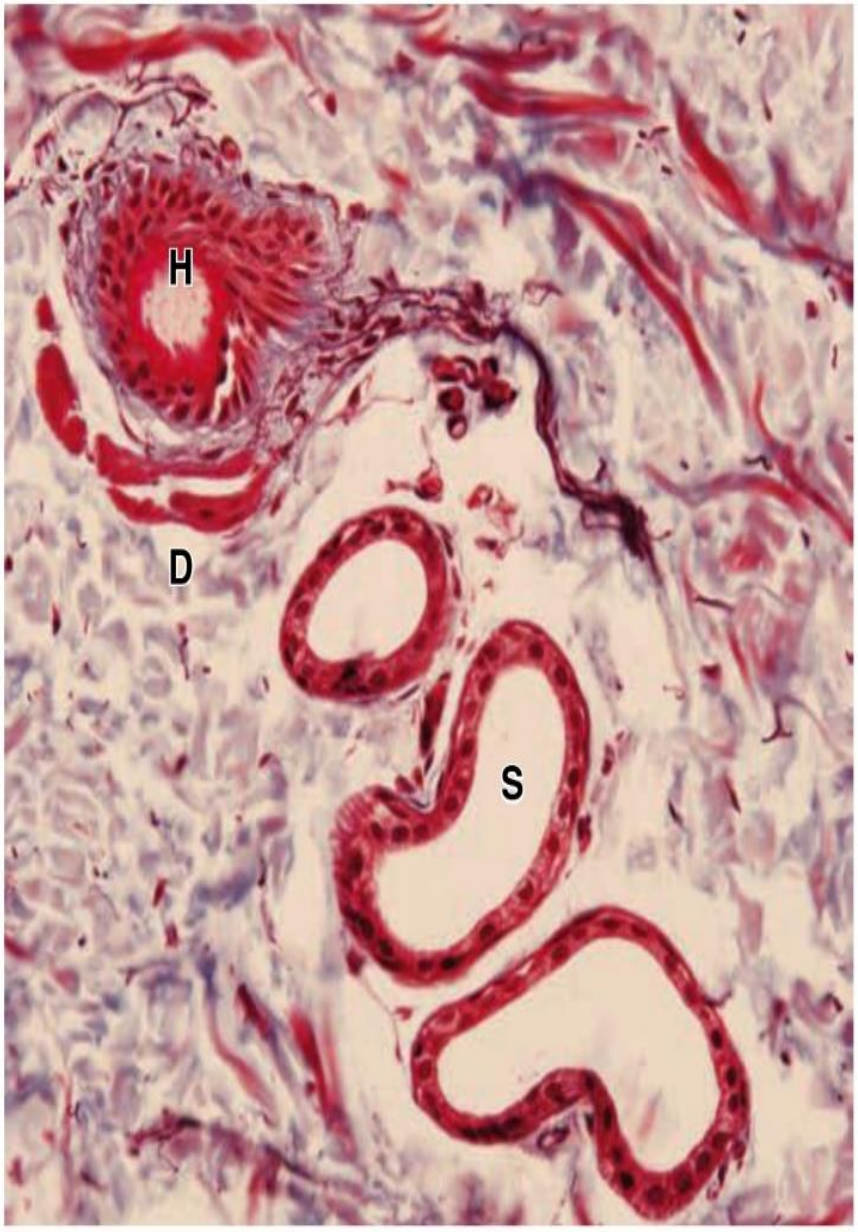
(a) Histologically eccrine glands have small lumens in the secretory components (**S**) and ducts (**D**), both of which have an irregular stratified cuboidal appearance. Both clear and acidophilic cells are seen in the stratified cuboidal epithelium of the secretory units. The box indicates an area 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)

Nails:

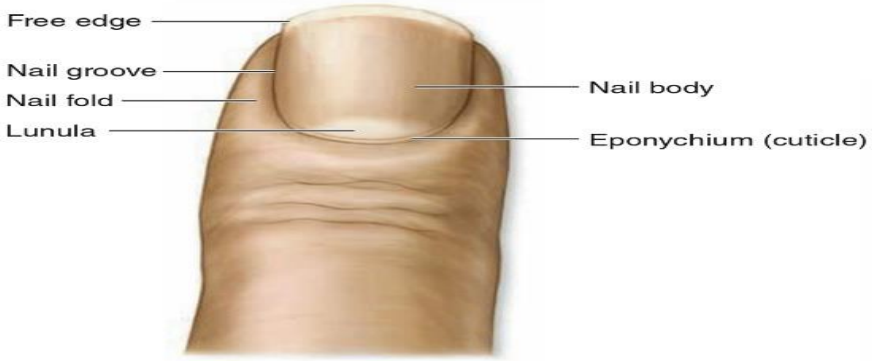
- Produced by cells in the epidermis
- Nail plate (body): visible portion
- Nail root: located under cuticle
- Lunula: half moon crescent shaped white portion under cuticle
- Nail bed: located under nail plate
- Hypoxia: decr. oxygen in blood, nail bed will turn blue-cyanosis

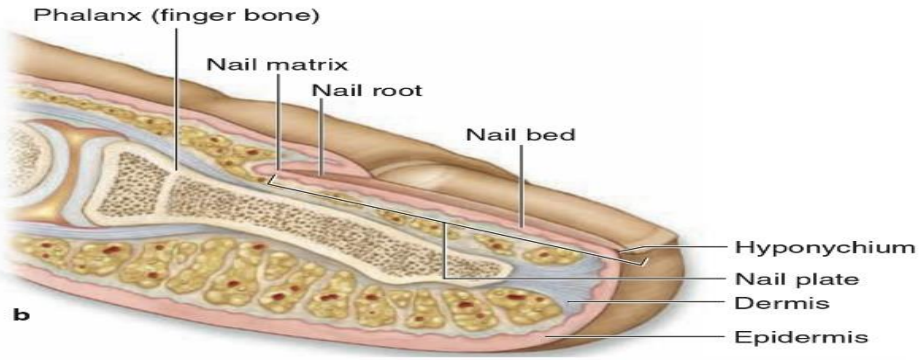
FIGURE 18–19 Apocrine sweat glands.

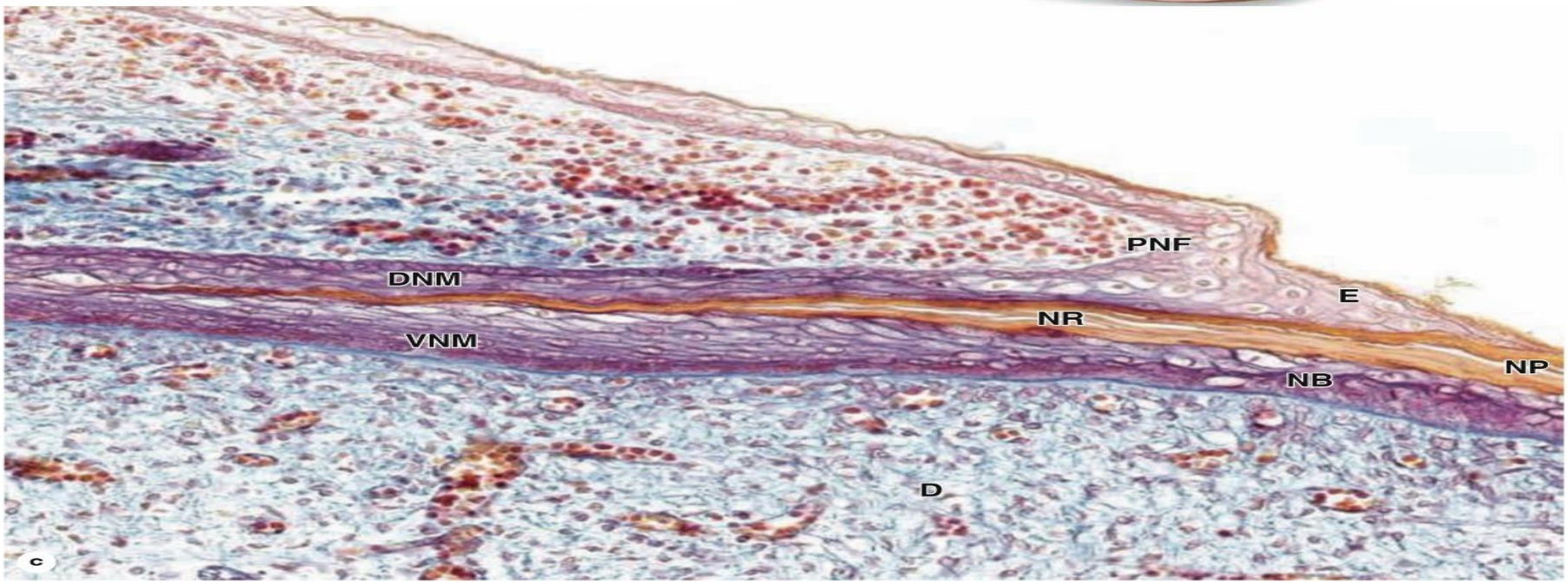


The secretory portions (**S**) of apocrine sweat glands have lumens that are much larger than those of eccrine sweat glands. The ducts (**D**) of apocrine glands also differ from those of eccrine glands in opening into hair follicles (**H**) rather than to the epidermal surface. (X200; Mallory trichrome)

FIGURE **18–15** **Nails.**





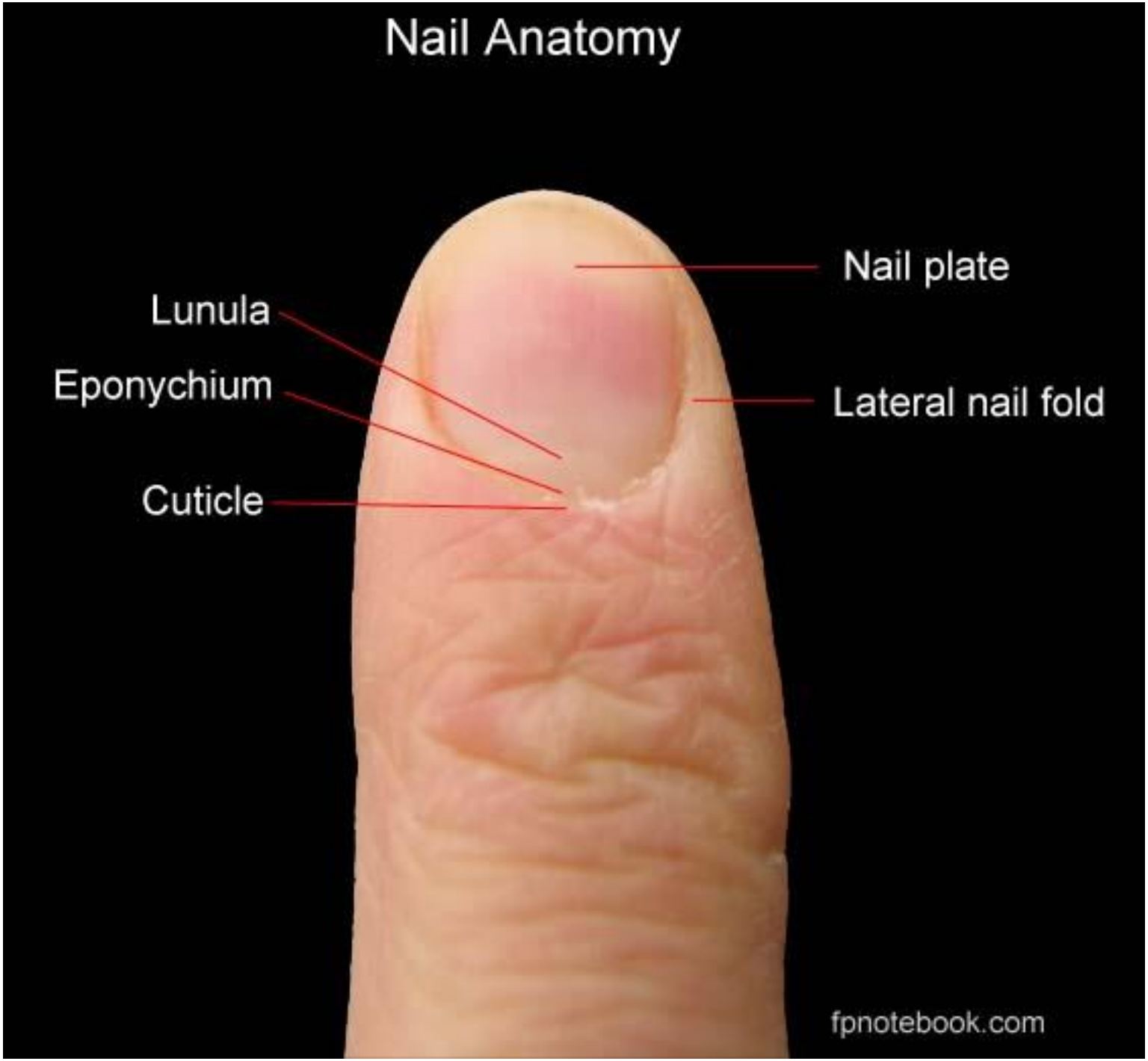


Nails are hard, keratinized derivatives formed in a process similar to that of the stratum corneum and hair.

(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)


Nail Anatomy
Nail plate
Lunula
Eponychium
Lateral nail fold
Cuticle
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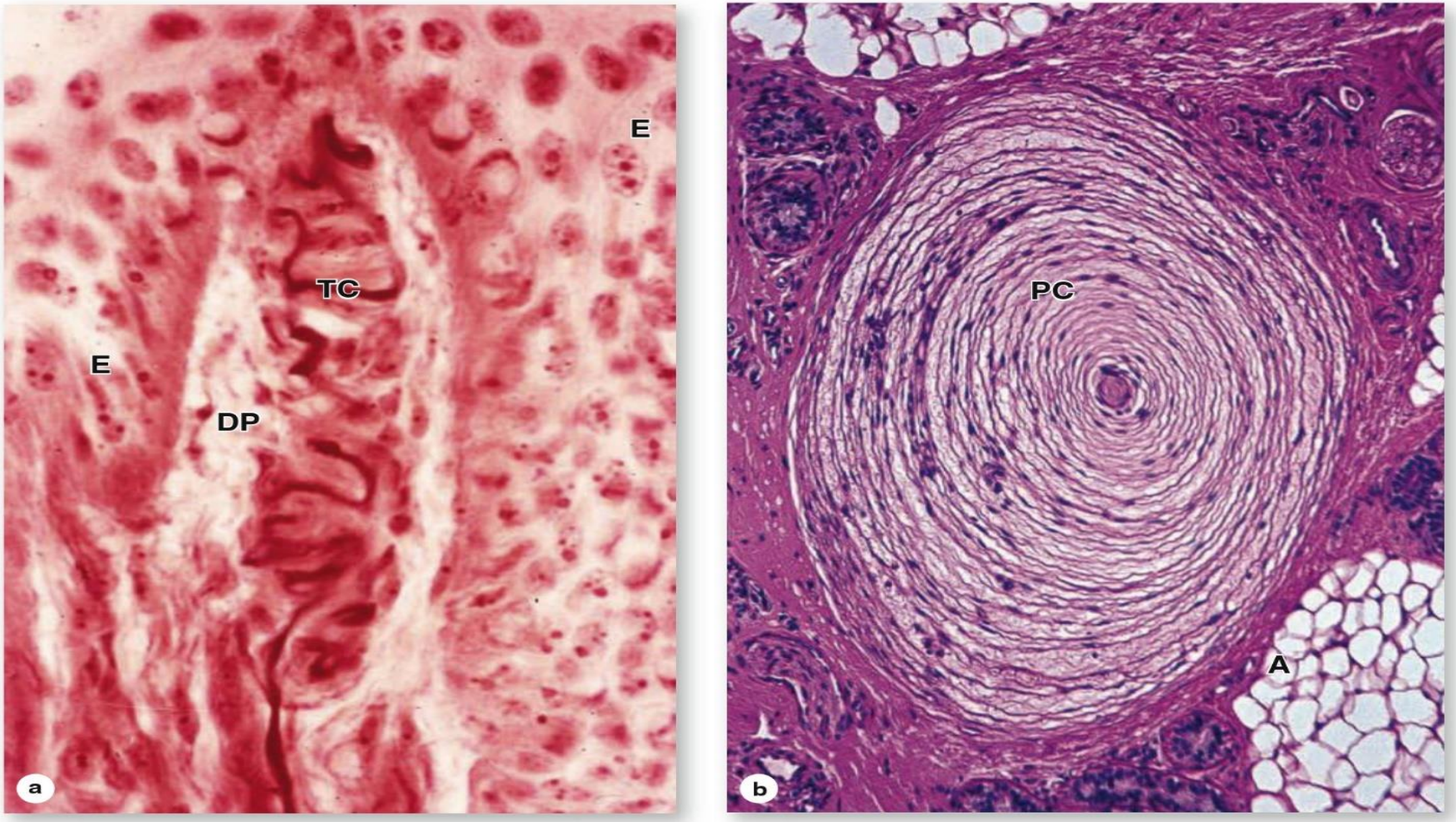
Nerve endings:

- Exteroceptors (stimulus outside of body)
  - Pacinian (lamellated) corpuscles: deep pressure and stretch
  - Meissner's (tactile) corpuscles: light touch, vibration and discriminative touch.
  - hair root plexus
  - free (naked) nerve endings: nociceptors (pain) and thermoreceptors (hot – deep and cold- surface)
  - Ruffini's corpuscles: deep pressure

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

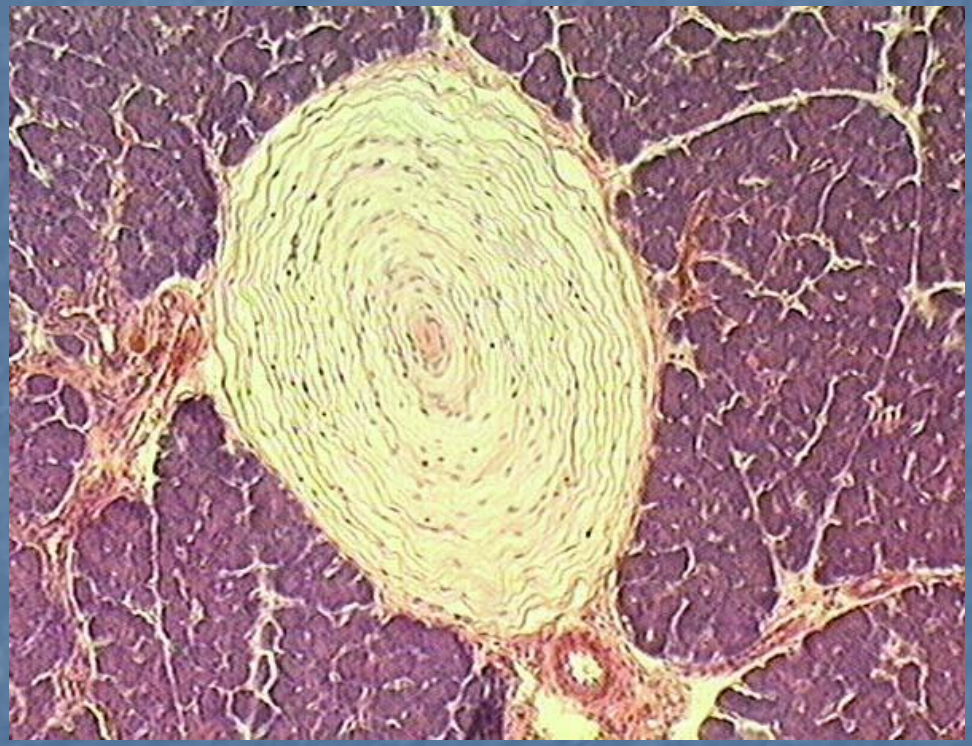


Micrographs show the two most commonly seen sensory receptors of skin.

(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)

Pacinian corpuscle



- Hypodermis
  - called subcutaneous, Sub-Q or superficial fascia
  - anchors skin to underlying structures
  - contains adipose tissue and blood vessels
  - common site for injection


Thank you