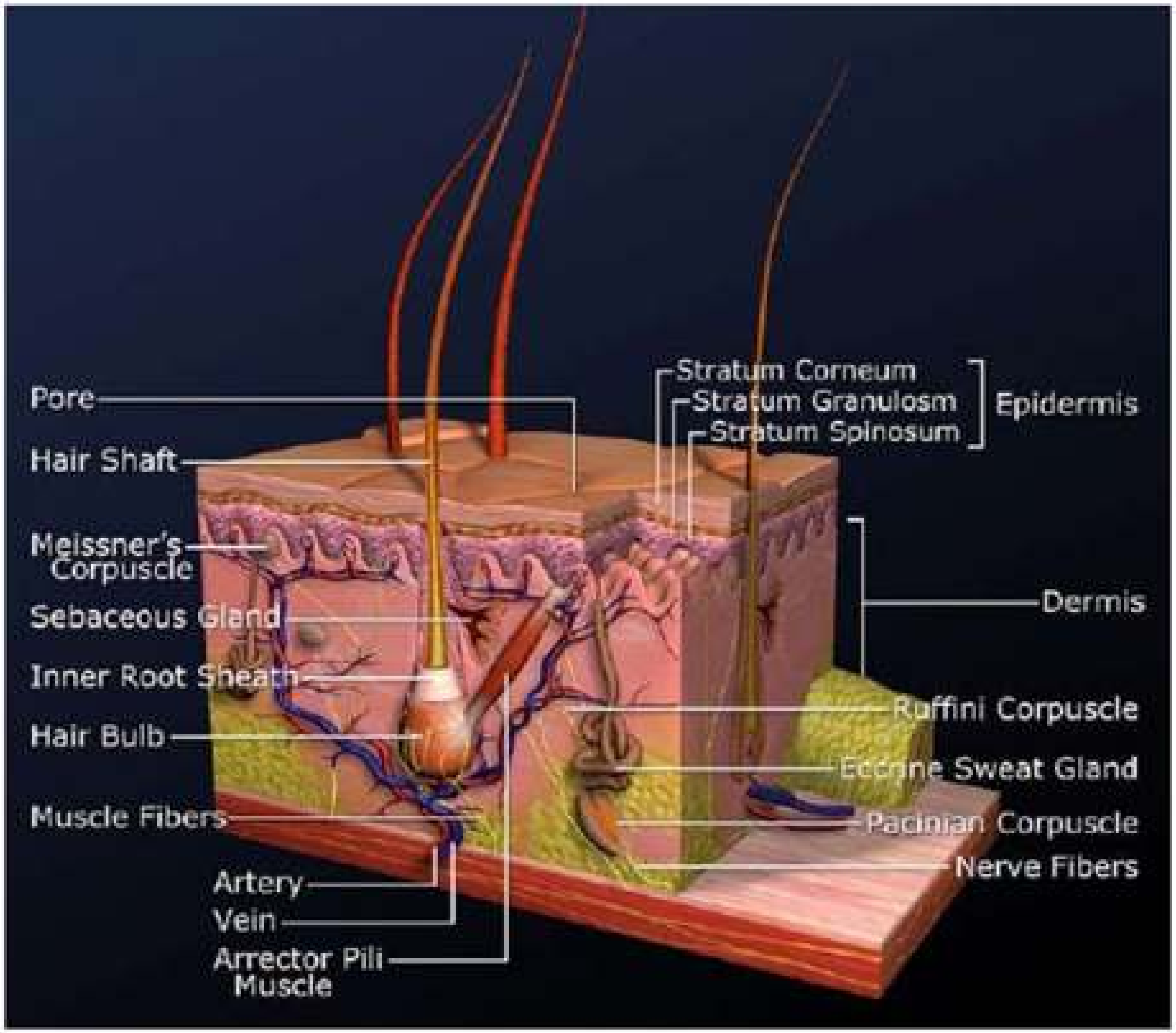
Integumentary system

Overview of the Integument

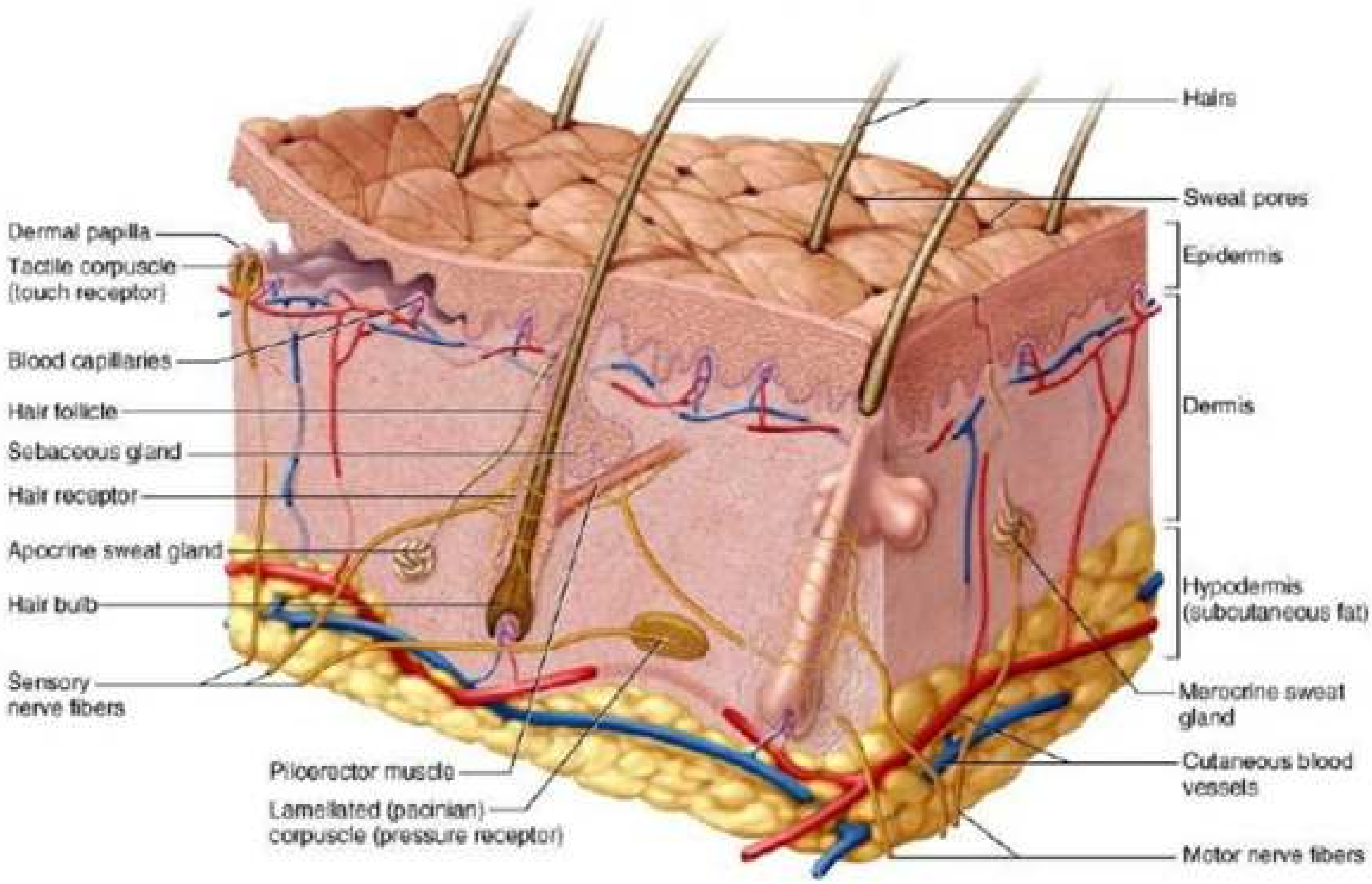
- Largest organ (15% of body weight)
- Surface area of 1.5-2 m^2
- Epidermis
  - keratinized stratified squamous epithelium
- Dermis
  - connective tissue layer
- Hypodermis
- Thickness variable, normally 1-2 mm
  - dermis may thicken, up to 6 mm
  - stratum corneum layer increased
    - calluses on hands and feet

Integumentary System



Andrew McCaskill - ICS

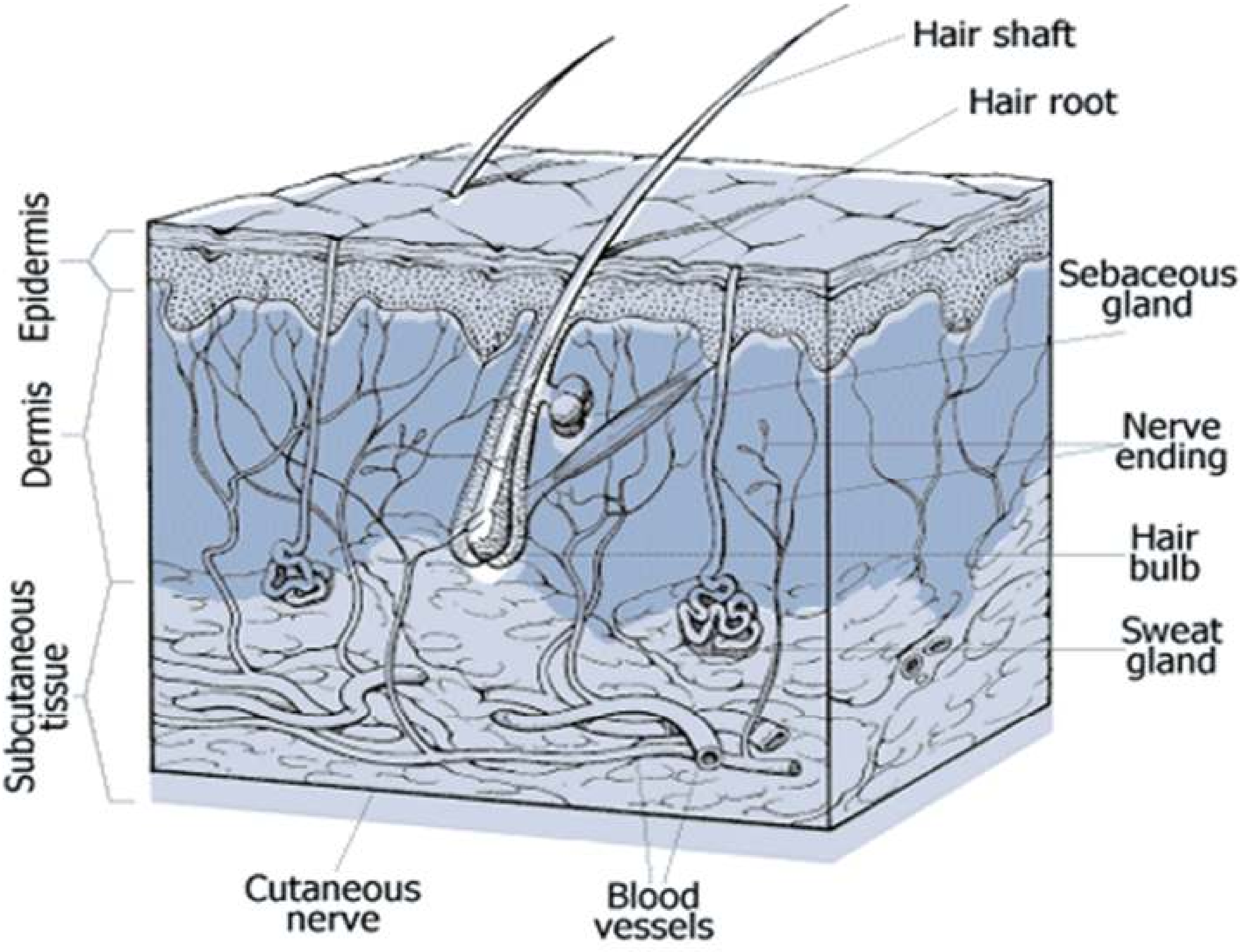
Structure of the Skin



Skin Main Functional Areas

The skin can be divided into four main functional areas:

- **epidermis** – the major protective layer derived from the fetal ectoderm;
- **dermis** – the major support layer – of mesodermal original;
- **hypodermis -** subcutaneous fat area **–** of mesodermal origin
- **skin appendages -** composed of cells derived from both ectoderm and mesoderm – hair follicle, sebaceous gland, apocrine sweat gland, eccrine sweat gland, and nails.



Hair shaft
Hair root
Sebaceous gland
Nerve ending
Hair bulb
Sweat gland
Epidermis
Dermis
Subcutaneous tissue
Cutaneous nerve
Blood vessels

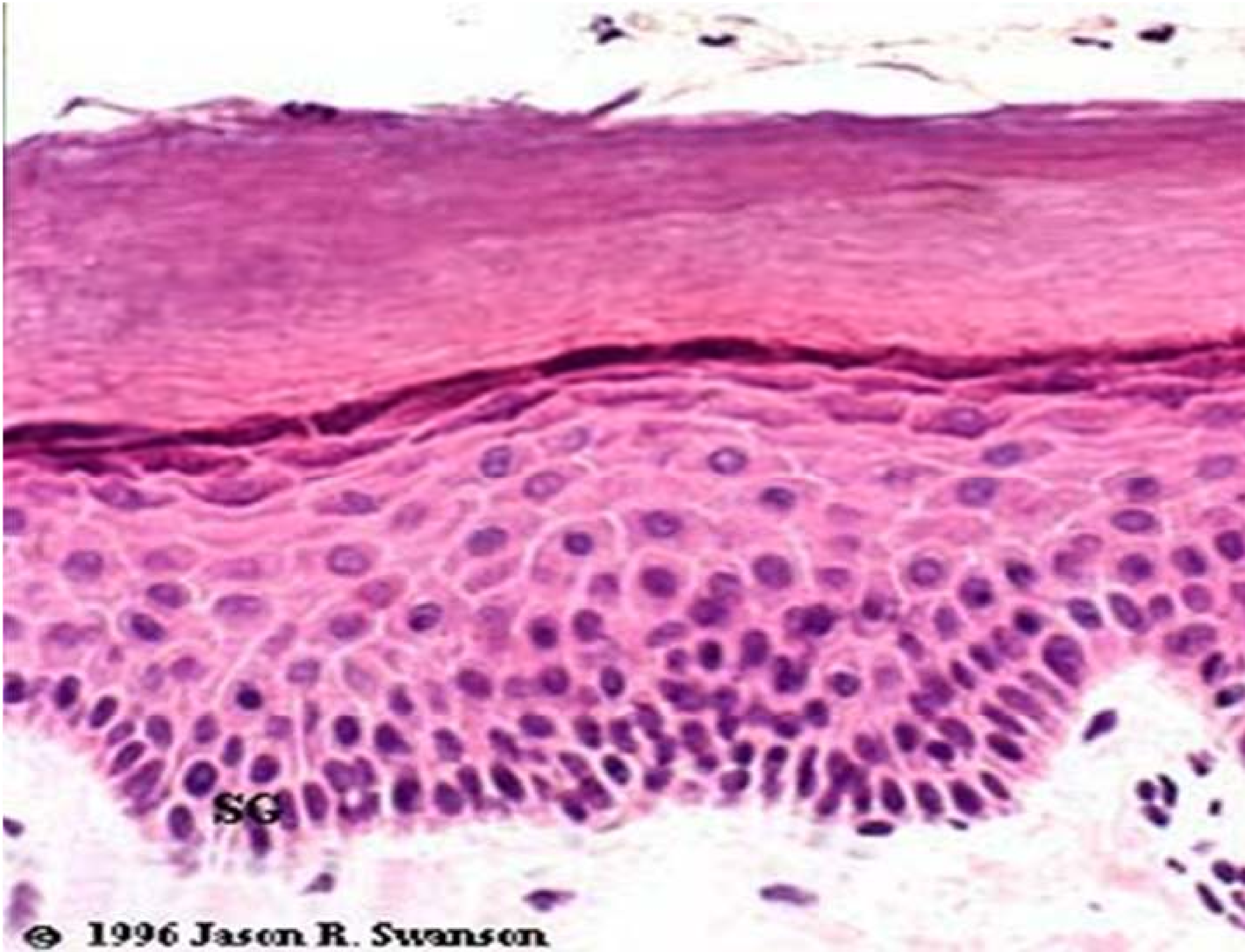
The Epidermis

Four main layers and sometimes another one additional :

- **cornified or horny layer** - outer non-nucleated barrier layer;
- **granular layer –** the zone where epidermal nuclei disintegrate;
- **spinosus or prickle cell layer –** the bulk of the living epidermal keratinocytes;
- **bazal layer –** the only keratinocytes in normal epidermis which undergo cell division.
- These layers are best seen if a piece of thick, weight-bearing skin, such as that from the sole of the foot, is examined under the microscope. In this skin, a fifth layer can sometimes be seen just above the granular layer – **the stratum lucidum.**

Stratum Basale = S. germinativum

- Single layer cells on basement membrane
- Cell types in this layer
  - Stem cells
    - Undergo mitosis to produce keratinocytes
  - Keratinocytes
    - Migrate toward skin surface and replace lost epidermal cells
  - Melanocytes
    - Synthesize and distribute melanin among keratinocytes
    - Distribute melanin through cell processes
    - Keratinocytes accumulate melanin on their "sunny side"
    - Equal numbers in all races
      - Differences in skin color due to differences in rate of production and how clumped or spread out melanin is
  - Merkel cells are touch receptors
    - form Merkel disc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Stratum Spinosum

- Several layers of keratinocytes
  - Some deeper keratinocytes continue to divide but superficial cells don't
  - Begin to synthesize protein *keratin* which cause cells to flatten
  - appear 'spiny' due to shrinkage during histological preparation
  - Bound to each other by desmosomes and tight junctions
- Contains dendritic (Langerhans) cells
  - macrophages from bone marrow that migrate to the epidermis


SS
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Stratum Granulosum

- 3 to 5 layers of flat keratinocytes; stopped dividing
- Contain keratinohyalin granules (hence its name)
  - combine with filaments of cytoskeleton to form keratin
- Produces lipid-filled vesicles that release a glycolipid by exocytosis to waterproof the skin
  - forms a barrier between surface cells and deeper layers of the epidermis
  - cuts off surface strata from nutrient supply


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Stratum Lucidum

- Thin translucent zone seen only in thick skin
- Keratinocytes are packed with keratin
- Cells have no nucleus or organelles


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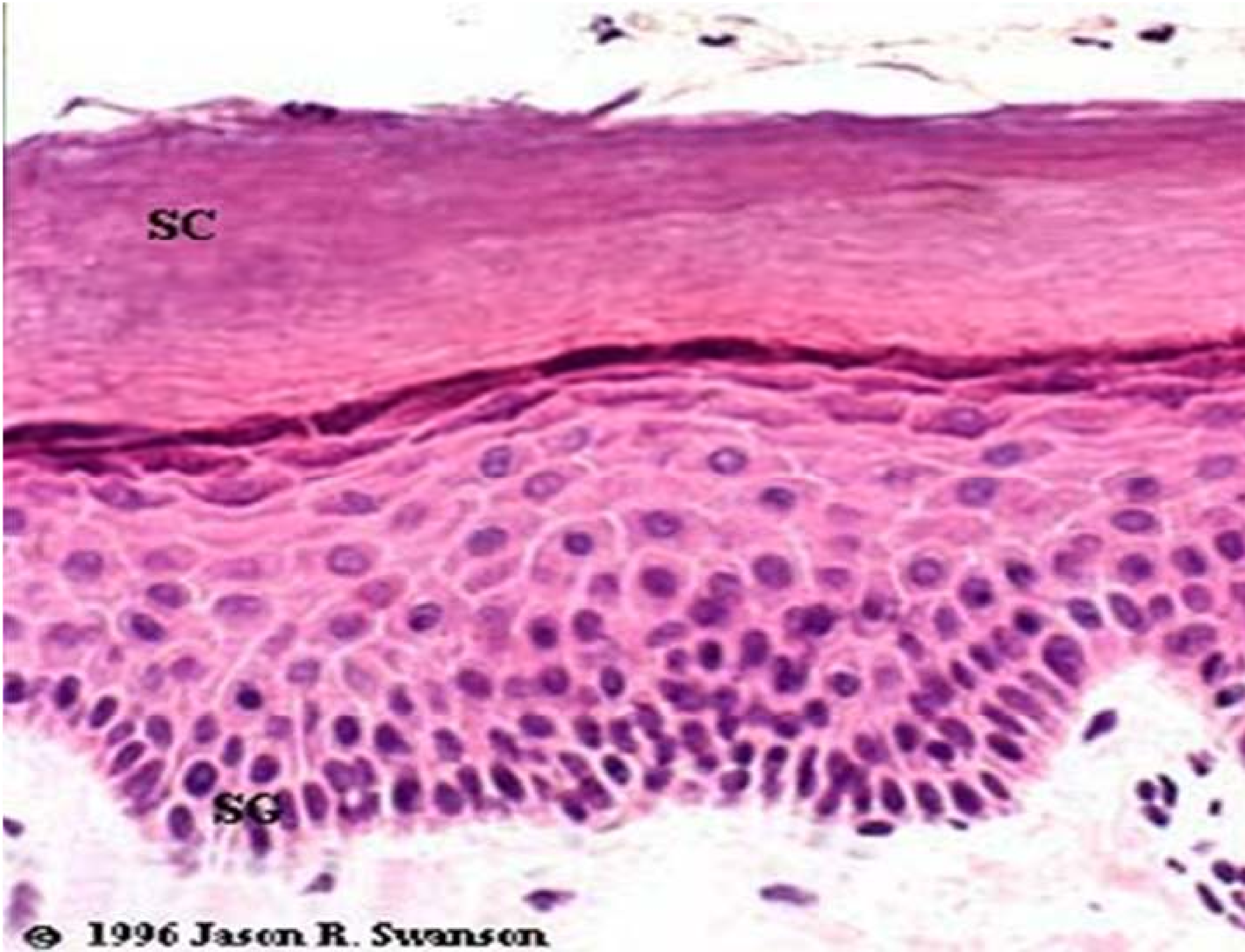
Stratum Corneum

- Up to 15-30 layers of dead, scaly, keratinized cells
  - Keratinization (cornification) - formation of protective, superfifcial layers of cells filled with keratin
  - Occurs on all exposed skin surfaces except anterior surface of eyes
  - Surface cells flake off (exfoliate) in sheets be-cause they are tightly interconnected by des-mosomes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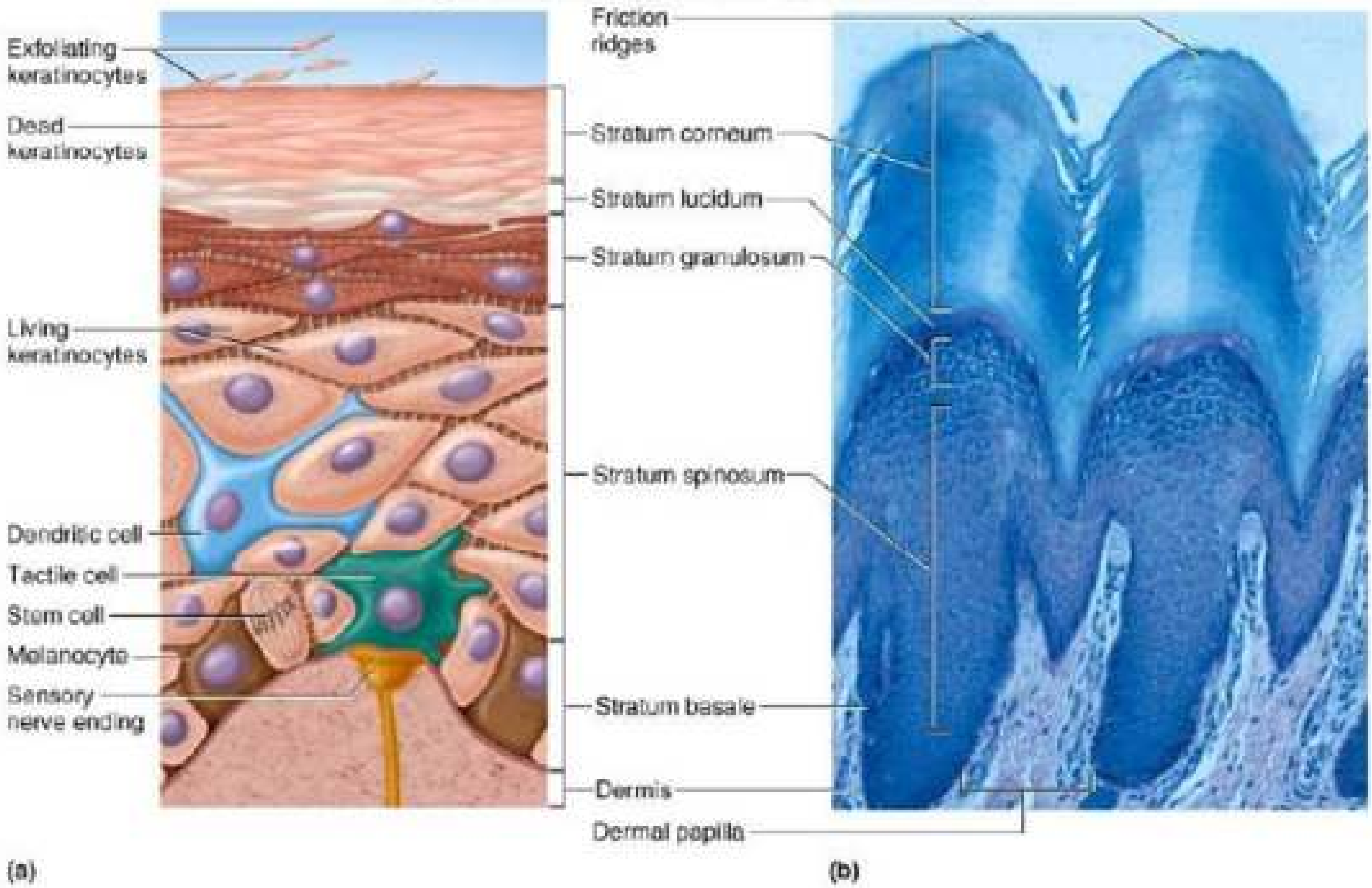
Cell Types Seen in the Epidermis

- **keratinocyte** – the main cell type; basal keratinocytes are a kind of stem cells
- **melanocyte** – found in the basal layer, the pigment-producing cell;
- **Langerhans cell** – found in the mid-dermis – an important immunologically competent cell;
- **Merkel cell** – in the basal layer – member of the amine precursor uptake and decarboxylation (APUD) - tactile receptor cells

Cell and Layers of the Epidermis



The keratinocyte

- **90%** of epidermal cells are keratinocytes
- In normal skin, keratinocyte **division** takes place **only in the basal layer**
- After cell division, one daughter **keratinocyte** remains in the basal layer and the other **moves upwards through the epidermis**.
- The keratinocyte is committed to **terminal differentiation and death**.
- Within the prickle cell layer, highly specialized cellular bridges, called **desmosomes** connect the keratinocytes to each other.
- There are **no desmosomes** between keratinocytes and **melanocytes, or Langerhans cells, or Merkel cells**.
- There are **hemidesmosomes** between the basal layer keratinocytes and the underlying basement membrane.
- **In the granular layer**, the living keratinocytes are involved in a complex series of biochemical changes during which **the cell nuclei disintegrate**, forming the **keratohyaline granules** seen in the cytoplasm.
- **The outermost layer** is the non-nucleate, **DEAD,** stratum corneum, or cornified layer.

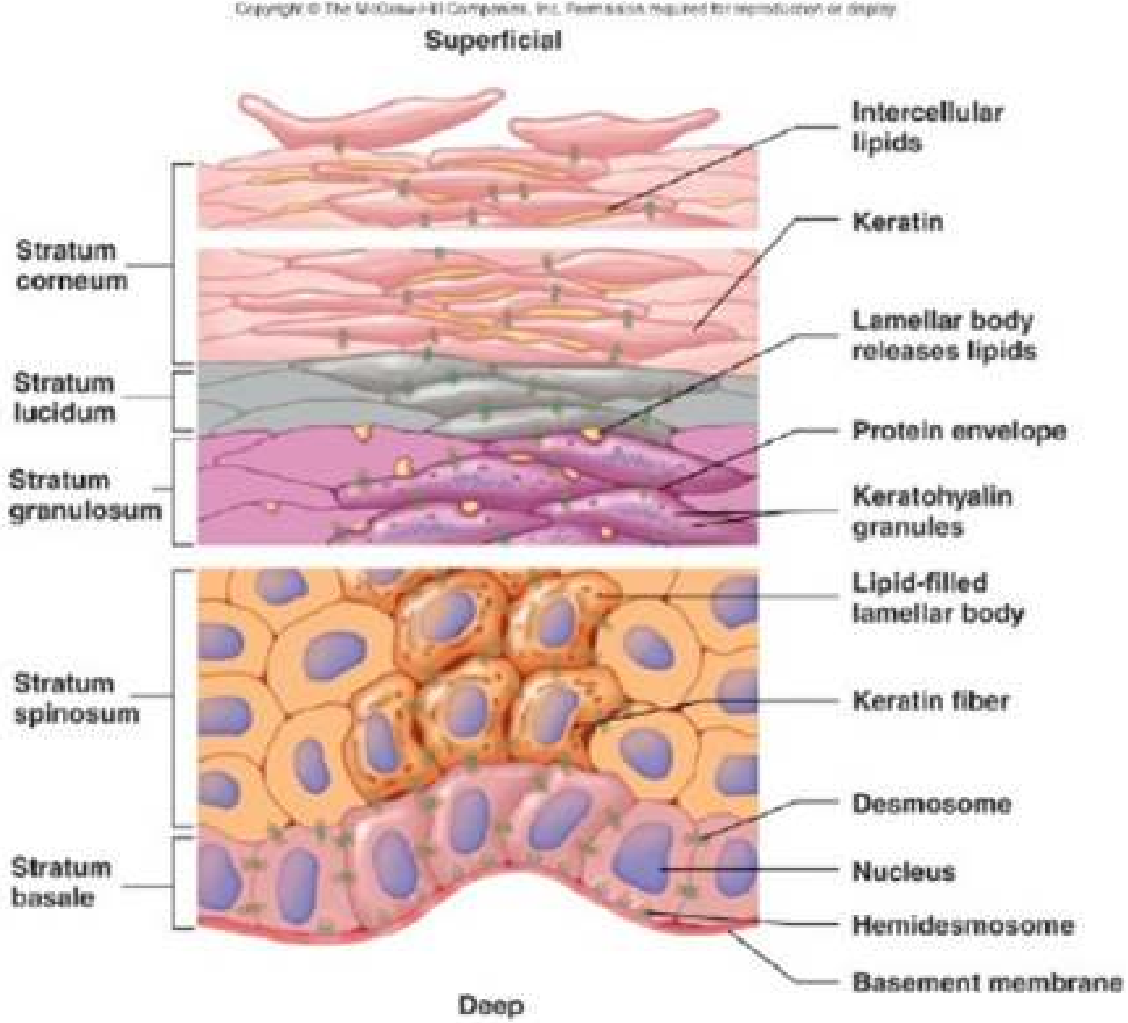
Epidermis
Development and Maturation

- Development and maturation of normal healthy epidermis in this pattern is called **ortokeratosis,** and produced an outer layer of non-nucleated, dead, flat keratinocytes.
- In some diseases the maturation pattern is different, and there is no granular layer, but an outer layer of nucleated squamous cells - that pattern is **parakeratosis (**psoriasis**).**
- The transit time – turnover – for keratinocyte in the basal layer of normal skin to reach the outer surface is around 28-30 days (in psoriasis - 8-10 days).

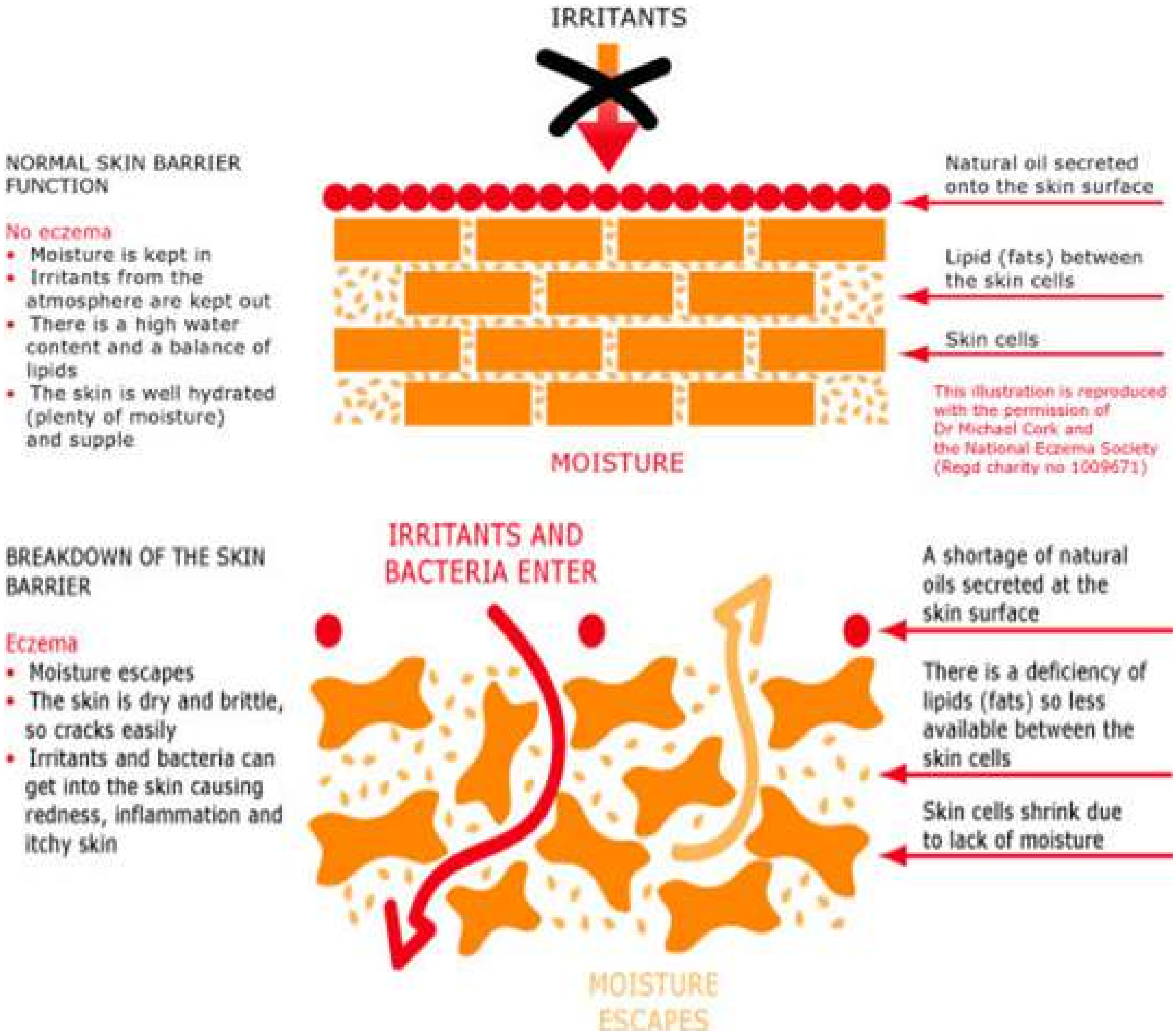
The Epidermis Strength

- The strength of the epidermis depends on the cohesion of the keratinocytes.
- They produce a structural protein, alpha-keratin, which aggregates to form **tonofilaments**.
- These tonofilaments are continuous with the desmosomes and are easily seen in the electron microscope as large cytoplasmic bundles.
- Another communication channel between keratinocytes is a gap junction, tiny channels, which connect the cytoplasm of neighboring cells to each other.

Epidermal Layers and Keratinization



Barrier function



Keratin synthesis abnormalities

- Normally, the basal layer of the epidermis synthesizes keratin 5 and 14
- Genetic disturbances in the genes coding for these keratin causes the disease epidermolysis bullosa simplex
- While the suprabasal keratinocytes synthesize keratin 1 and 10, and abnormalities give rise to bullous ichthyosiform erythroderma or epidermolytic hyperkeratosis.

ICAM; HLA-antigens

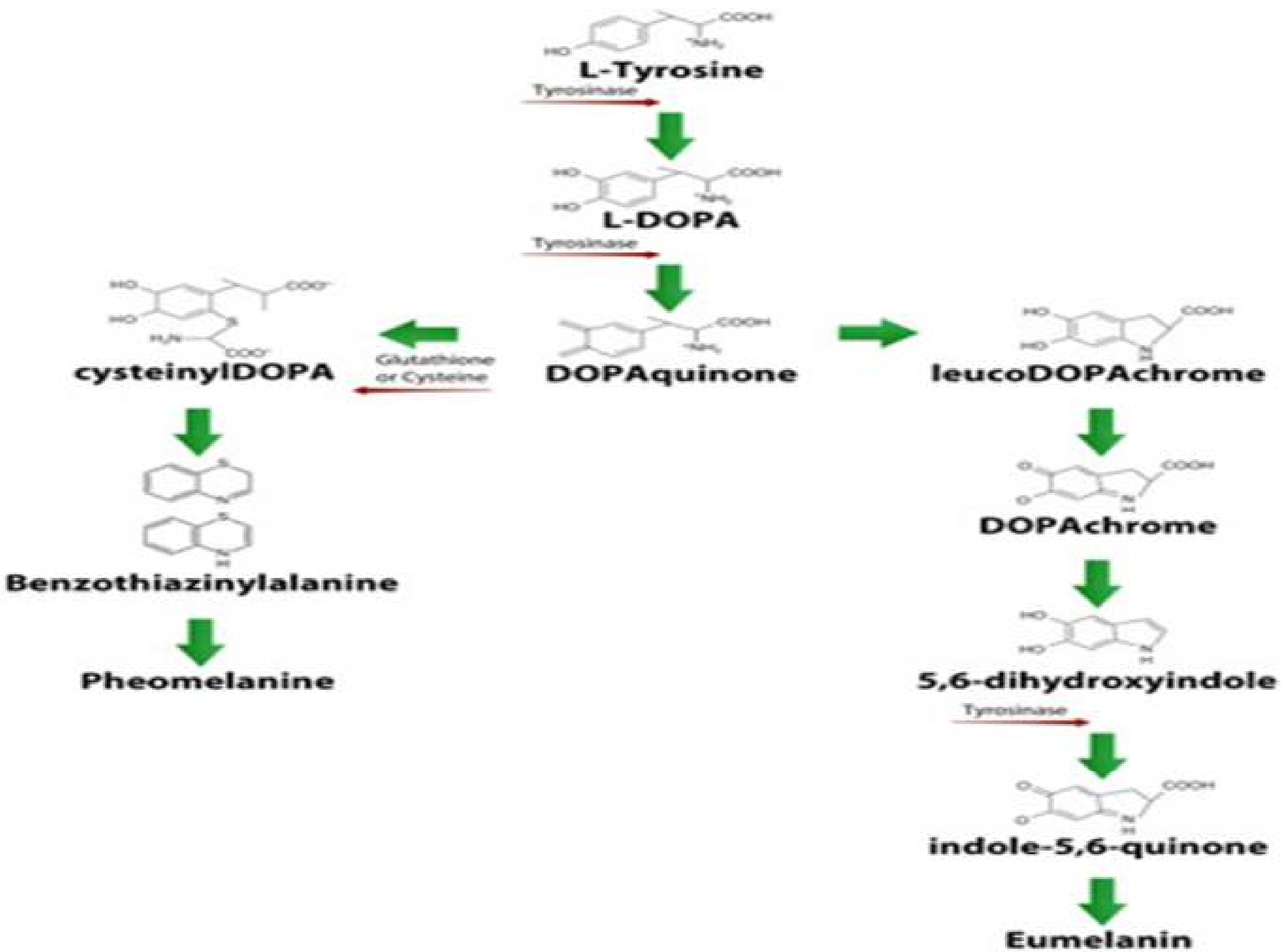
- **Cell adhesion molecules – ICAM –** is expressed on the surface of keratinocytes and forms one half of a ‘lock and key’ arrangement between these keratinocytes and lymphocytes.
- In the normal epidermis, the only cells that normally express the MHC class 2 antigens HLA-DR, -DP, and – DQ are the Langergans cells.

The melanocyte

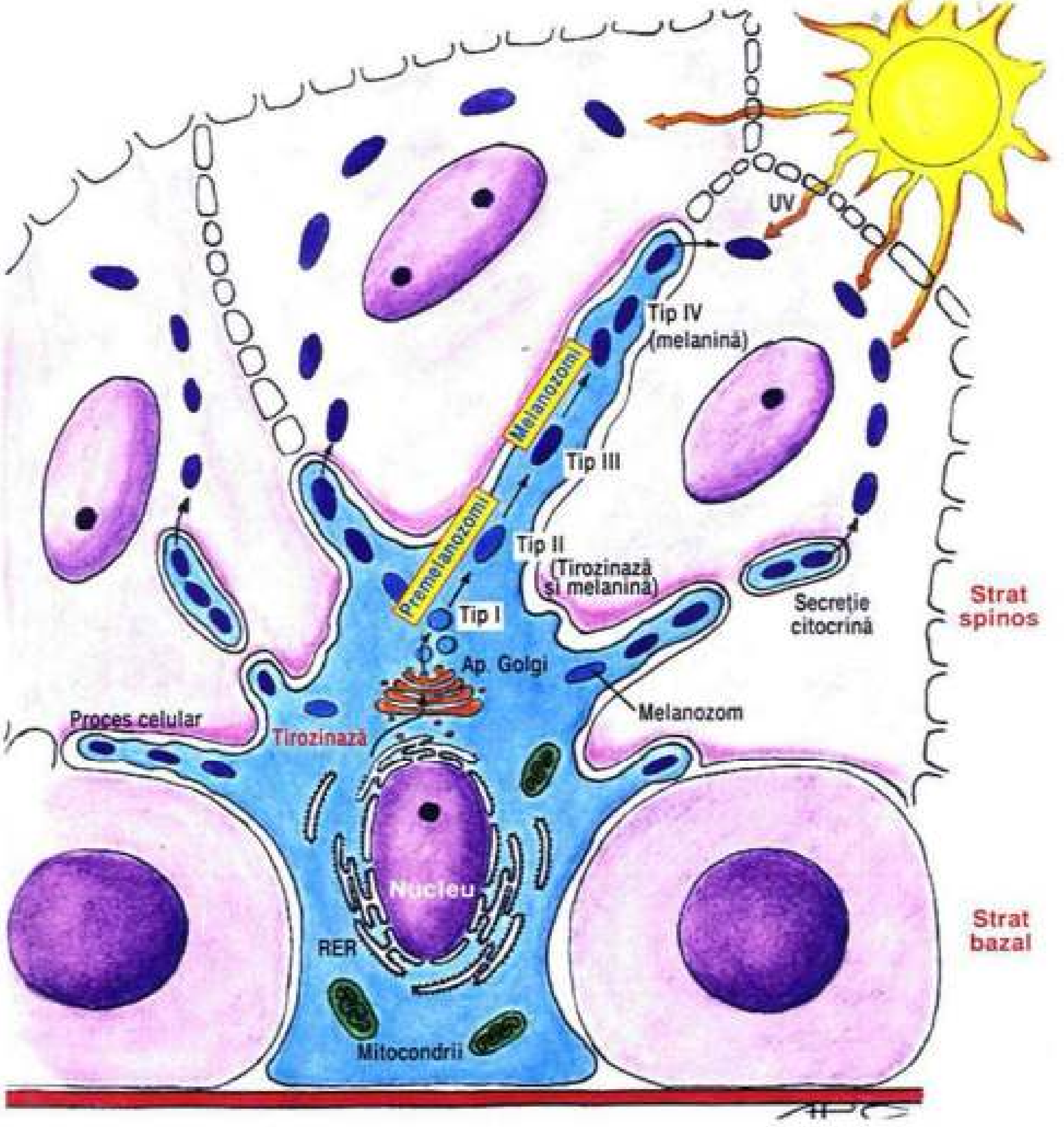
- The **melanocyte** has multiple dendrites and these dentritic processes stretch between adjacent keratinocytes.
- On facial skin there may be as many as one melanocyte for every five basal layer keratinocytes, but in the lower back skin this ratio is usually closer to one in 20.
- Numbers of melanocytes are the same in equivalent body sites in white and black skin, but the rate of production of pigment and its distribution is different.

Melanin synthesis

- Melanocytes synthesize the pigment **melanin**.
- Melanin granules are seen on ultrastructural examination as small, black, electron-dense, intracytoplasmic structures – the melanosomes.
- Tirosyne The pigment is formed from DOPA on premelanosomes and this biochemical reaction is catalyzed by the presence in the melanocyte of the enzyme dopa-oxidase and tyrosinase, which are not present in surrounding keratinocytes or other non-melanocytic cells.



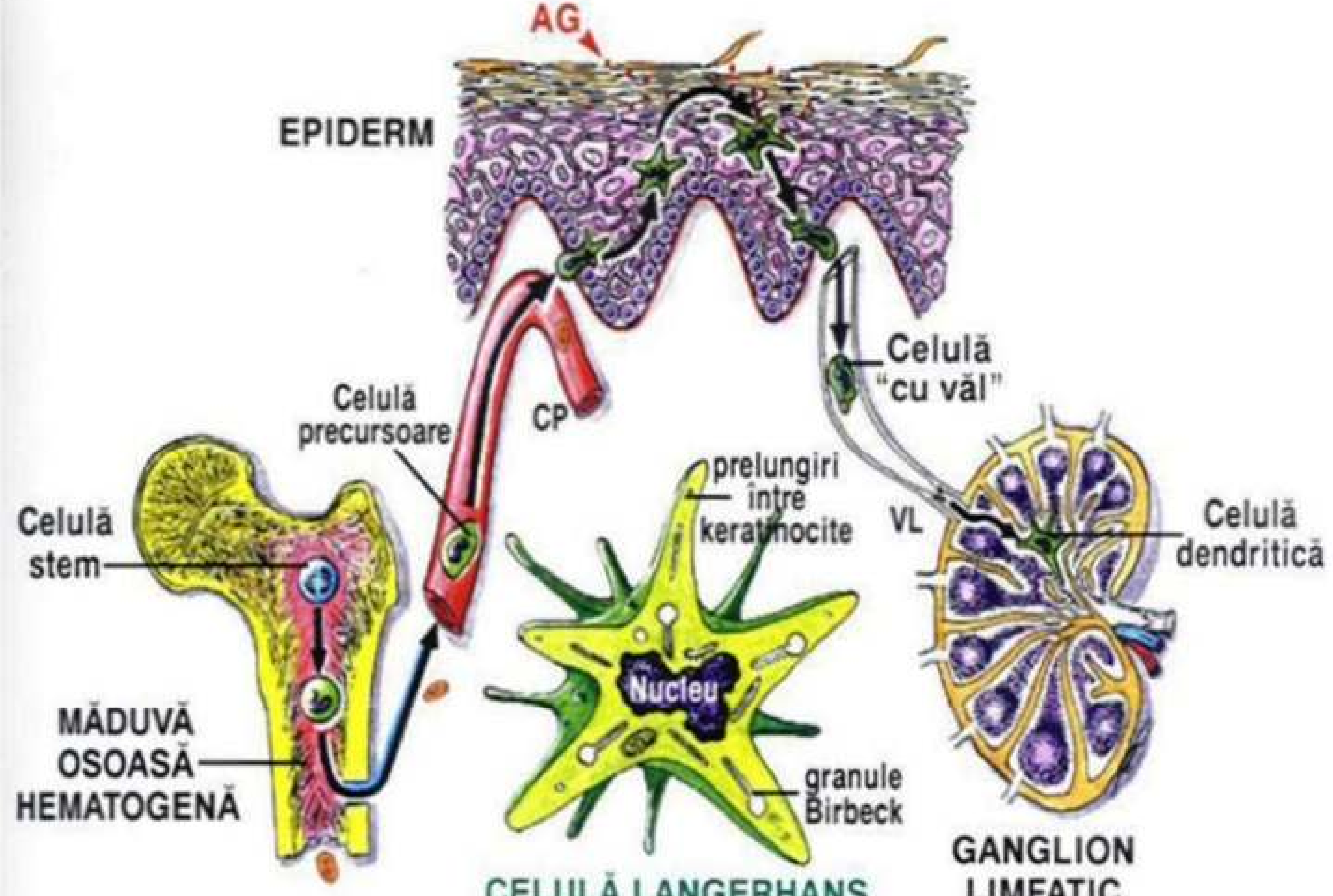
L-Tyrosine
Tyrosinase
L-DOPA
Tyrosinase
cysteinylDOPA
Glutathione or Cysteine
DOPAquinone
leucoDOPAchrome
Benzothiazinylalanine
Pheomelanine
DOPAchrome
5,6-dihydroxyindole
Tyrosinase
indole-5,6-quinone
Eumelanin



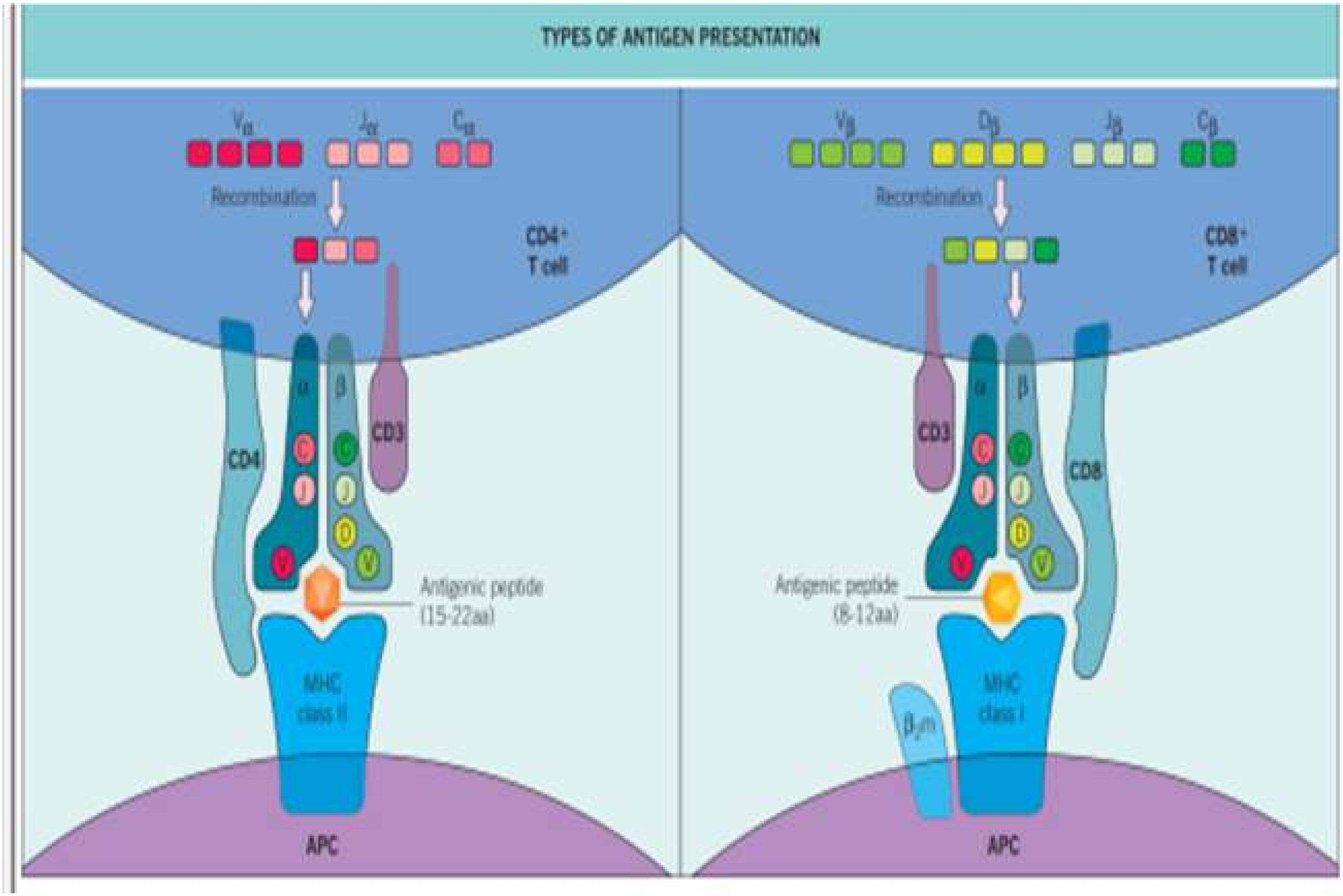
UV
Tip IV
(melanină)
Melanozomi
Premelanozomi
Tip III
Tip II
(Tirozinază
și melanină)
Tip I
Ap. Golgi
Secreție
citocrină
Strat
spinos
Proces celular
Tirozinază
Melanozom
Nucleu
RER
Mitocondrii
Strat
bazal

Other epidermal cells

- The **Langerhans cells** are immunologically competent and may act as antigen present cells. L.C. in normal skin is the only cell to express MNS class 2 antigens and carry receptors for complement.
- The **Merkel cells**– their exact normal function is not known but is thought to be related to cutaneous sensation.


AG
EPIDERM
Celulă
"cu văl"
Celulă
precursoare
CP
prelungiri
între
keratinocite
Celulă
stem
VL
Celulă
dendritică
Nucleu
MĂDUVĂ
OSOASĂ
HEMATOGENĂ
granule
Birbeck
GANGLION
LIMFATIC
CELULĂ LANGERHANS

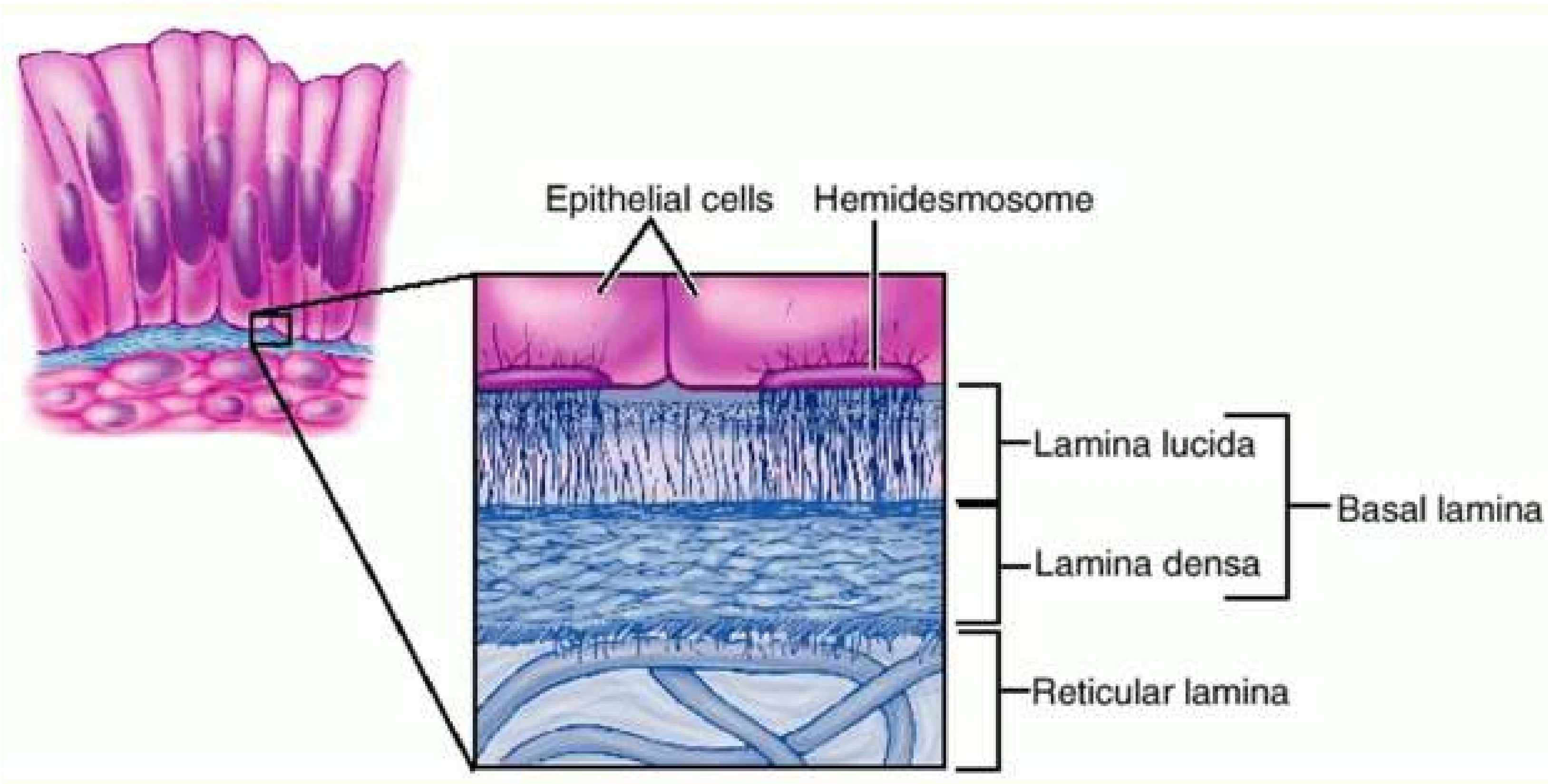
LC antigen presentation



The basement membrane

- The basement membrane divides the epidermis from the dermis, and is a complex multi-layered structure.
- Hemidesmosomes attach the basal layer keratinocytes to the lamina lucida (laminin here) area.
- Below this level is the sub-basal dense plate through which anchoring filaments (type 7 collagen here) connect the lamina lucida to the lamina densa (type 4 collagen here).

Basement membrane

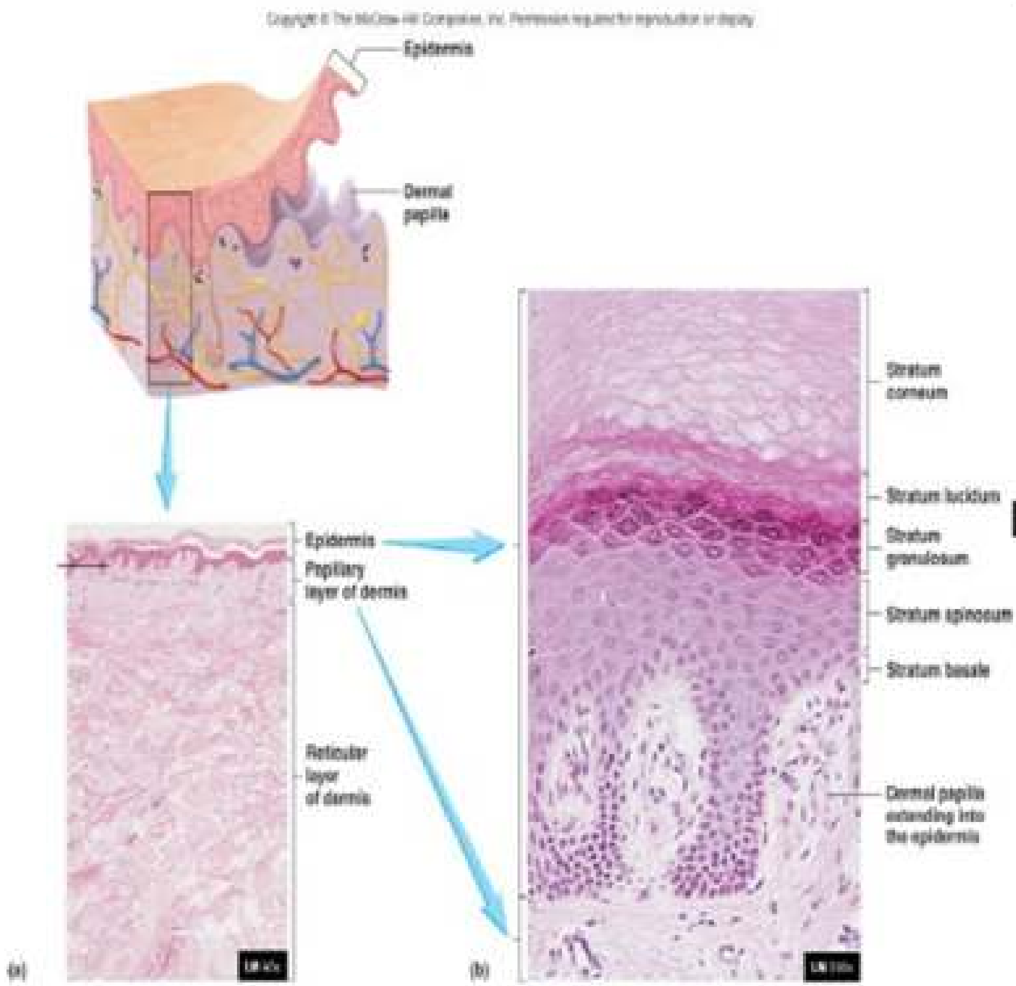


The dermis

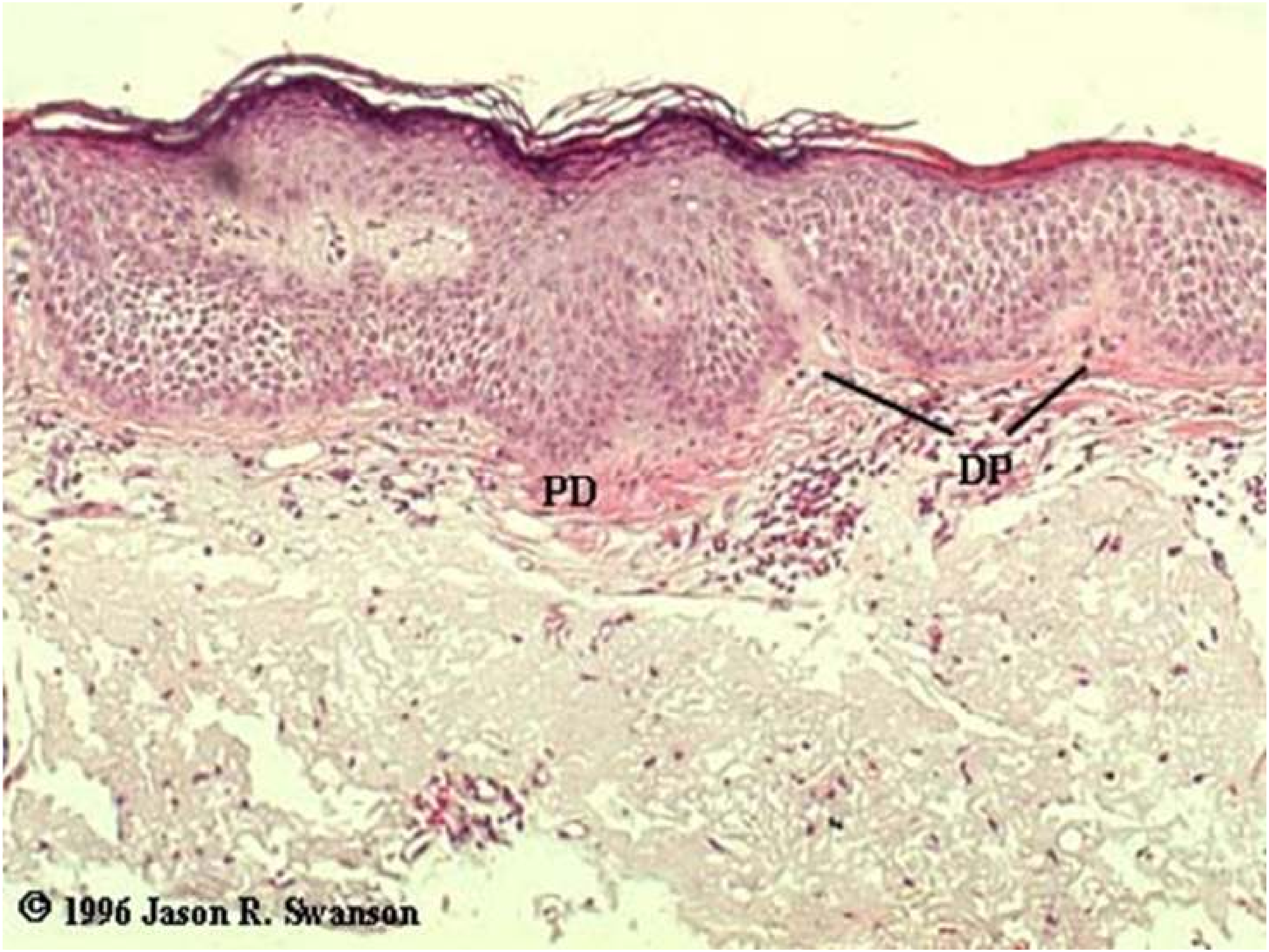
The dermis is organized into two distinct areas:

- **the papillary dermis** – superficial zone beneath the epidermis with thin, delicate colagen fibers and is highly vascularized;
- **the reticular dermis:** composes the bulk of the dermis, is less vascular and demonstrates thick, well-organized collagen bundles

Dermis



- Two layers of the dermis
  - **Papillary**. Superficial (outer) 1/5.
    - Areolar tissue with lots of elastic fibers.
    - Dermal papillae (Fingerprints)
    - Capillary beds.
    - Touch receptors (Meissner's), free nerve endings sensing pain
  - **Reticular**: Deep (inner) 4/5
    - Dense irregular C.T.
      - Collagen and elastic fibers.
      - Hair follicles, nerves, oil glands, ducts of sweat glands, other sensory receptors


PD
DP
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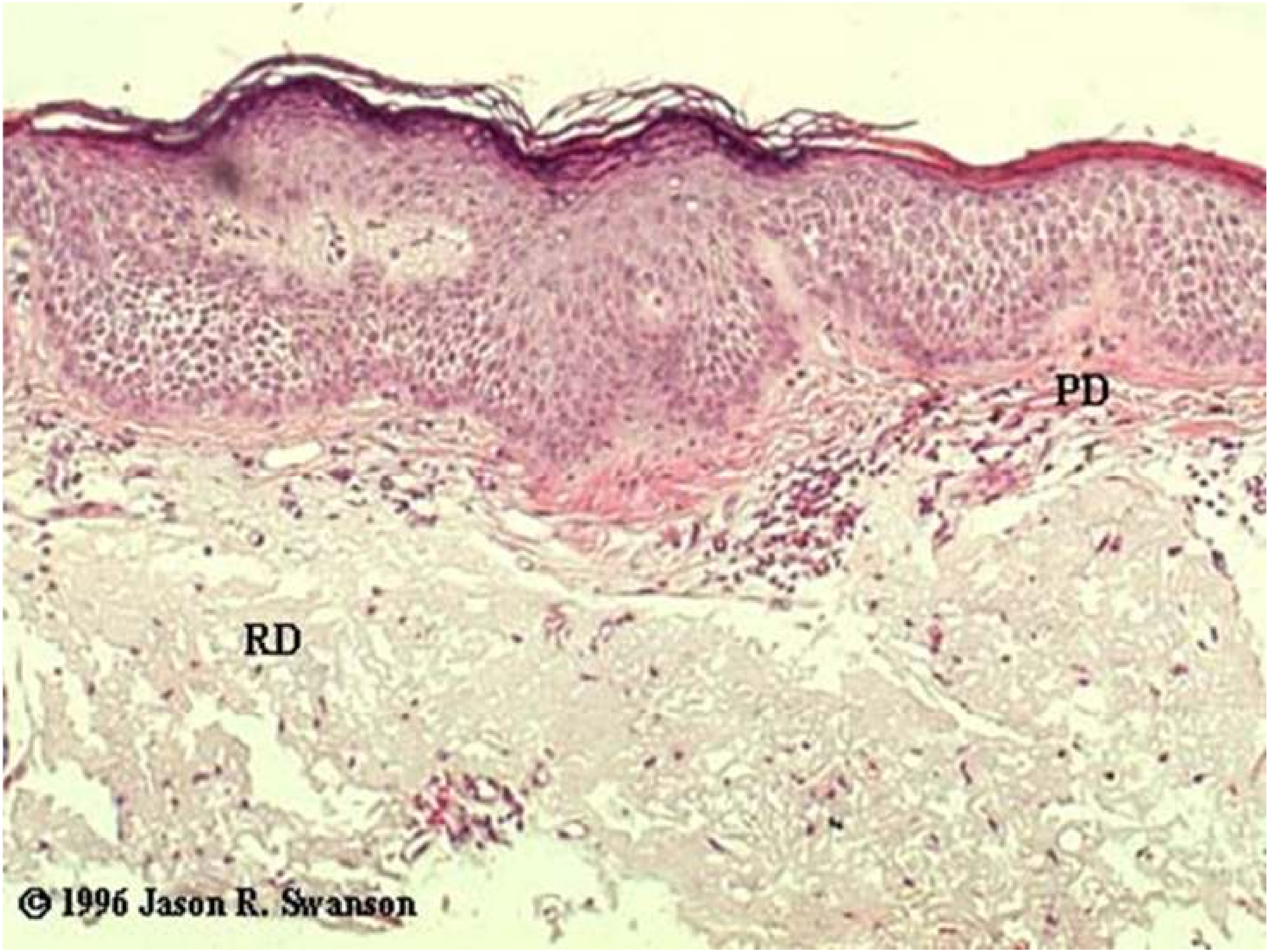
PD
RD
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Dermis Cells

There are three main cell types in the dermis:

- **the fibroblast** – responsible for making collagen, elastin and proteoglycans;
- **the macrophage** – acts as a general scavenger;
- **the mast cell** – an important cell in type 1 immunological reactions and interactions with the eosinophil
- the lymphocyte, polymorph, eosinophill cell – occasionally

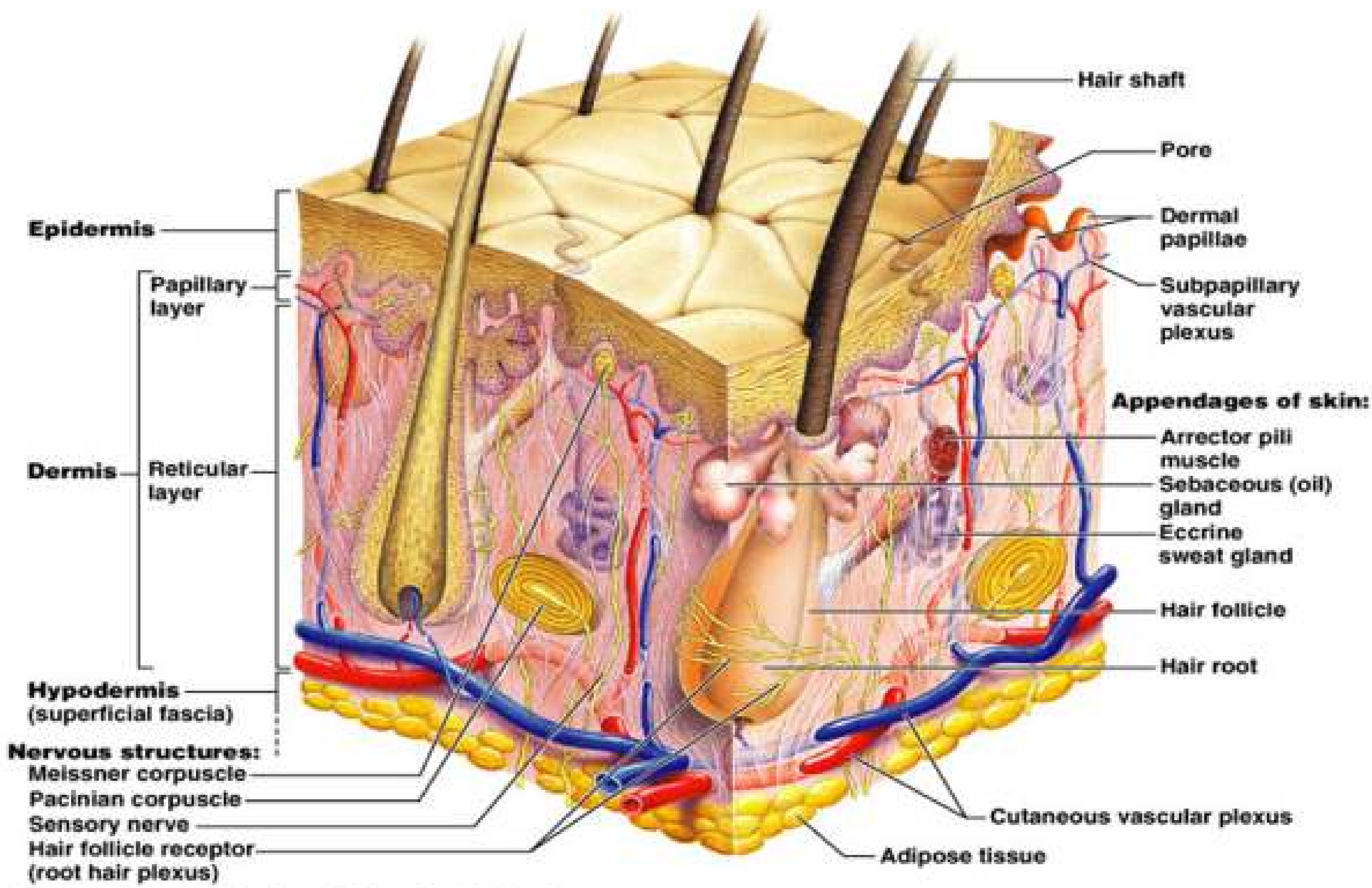
Components of the dermis

- Collagen fibers (90%) for resiliency
- Elastic fibers (10%) for elasticity
- Ground substance - proteoglycans (primarily hyaluronic acid) to maintain water within the dermis and compose amorphous ground substance around collagen and elastic fibers.

Other dermal components

- Vasculature - the blood supply to both epidermis and dermis is through a very rich anastomosing superficial and deep plexus of small blood vessels.
- Lymphatics - in normal skin the **lymphatic drainage system** is not visible, but this is also a profuse network, running from the reticular dermis to the local lymph nodes.
- Nerves – both free nerve endings and specialized receptors will be seen in the dermis. These nerve endings are important for the sense of touch, heat, cold, pain, itch mecanical stimuli. Striking specialized corpuscular receptors, the Pacinian’s and Meissner’s, serve as mechanoreceptors for pressure and vibration.
- Smooth and striated muscle in small quantities

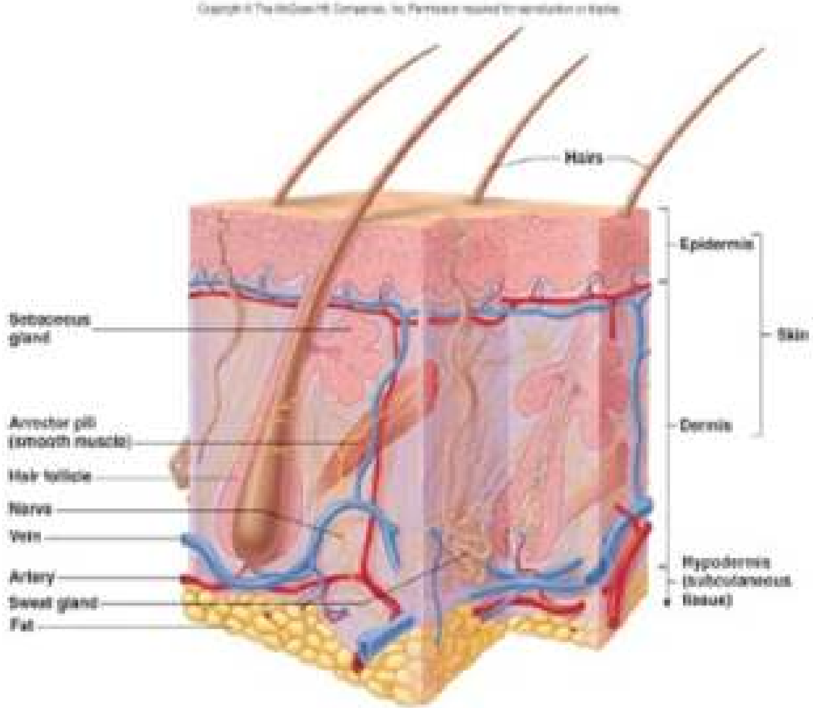
Dermis


Hair shaft
Pore
Dermal papillae
Subpapillary vascular plexus
Appendages of skin:
Arrector pili muscle
Sebaceous (oil) gland
Eccrine sweat gland
Hair follicle
Hair root
Cutaneous vascular plexus
Adipose tissue
Epidermis
Dermis
Papillary layer
Reticular layer
Hypodermis (superficial fascia)
Nervous structures:
Meissner corpuscle
Pacinian corpuscle
Sensory nerve
Hair follicle receptor (root hair plexus)

The subcutaneous fat - hypodermis

- The subcutis, or subcutaneous fat, is arranged into distinct fat lobules which are divided by fibrous septae composed primarily of collagen.
- Blood vessels, nerves and lymphatics are also found in the fibrous septae.

Hypodermis



- The subcutaneous tissue, superficial fascia
- Deep to the epidermis
- Mostly adipose tissue
- Functions:
  - Energy reservoir (fat)
  - Thermal insulation
  - Padding/cushioning
- Hypodermic injections (subQ)
  - Highly vascular

The skin appendages

- The pilosebaceous unit
- The eccrine sweat glands
- The nails.

The pilosebaceous unit includes the:

- **hair follicle**
- **sebaceous gland**
- **erector pili muscle**
- **apocrine gland** in some sites, for example axilla.

The hair follicle

- **Is** the result of interaction between downgrowth of fetal ectoderm, which will form the hair shaft, and the vascular hair bulb papilla, which is derived from fetal mesoderm.
- The hair shaft itself is a complex multilayered structures with an outer cortex and an inner medulla.
- There are three recognizable types of hair:

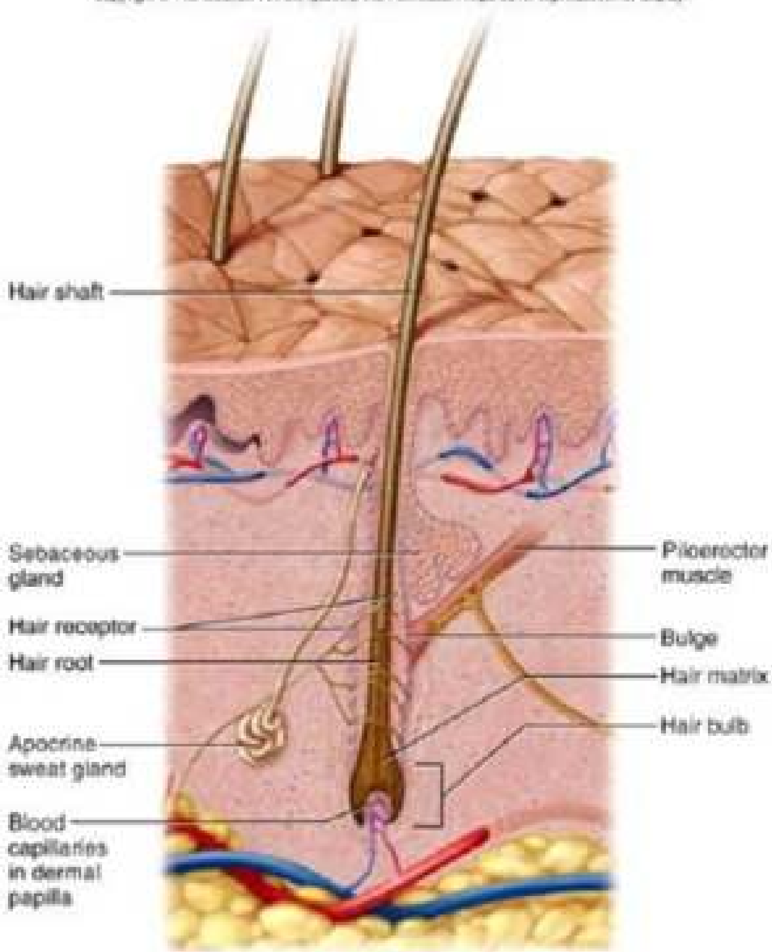
✓ the coarse terminal hairs of the scalp

✓ the androgen-dependent terminal hair on the male chin, in the axilla, and the pubic region

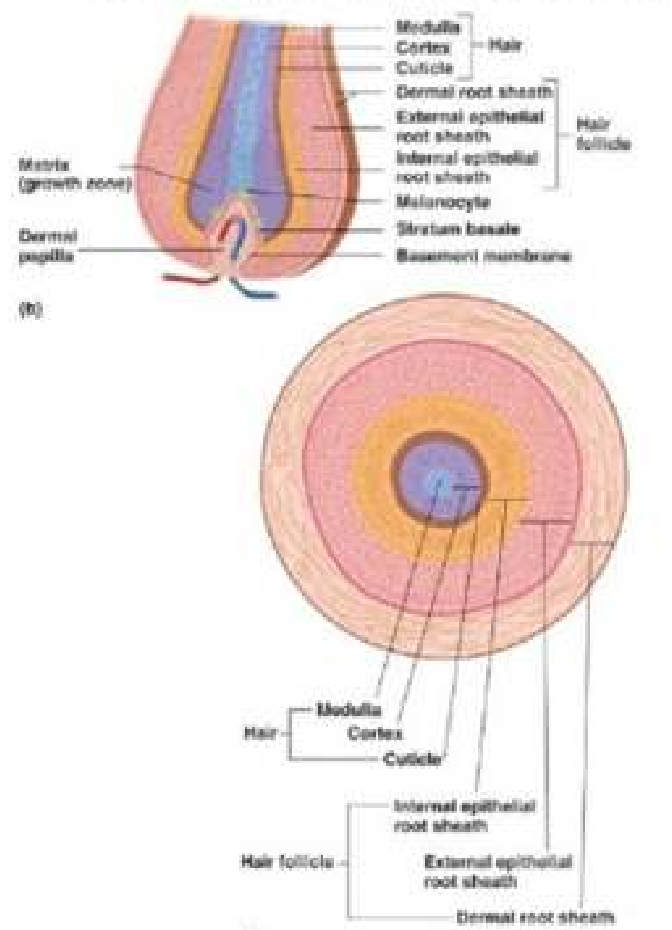
✓ and a fine growth vellous hair on all body sites.

- Three hair phases: anagen, catagen and telogen. At any time 80 per cent of scalp hair is growing in **anagen**, and the remaining 20 per cent either resting – in **catagen** – or being shed – in **telogen**.

Structure of Hair Follicle

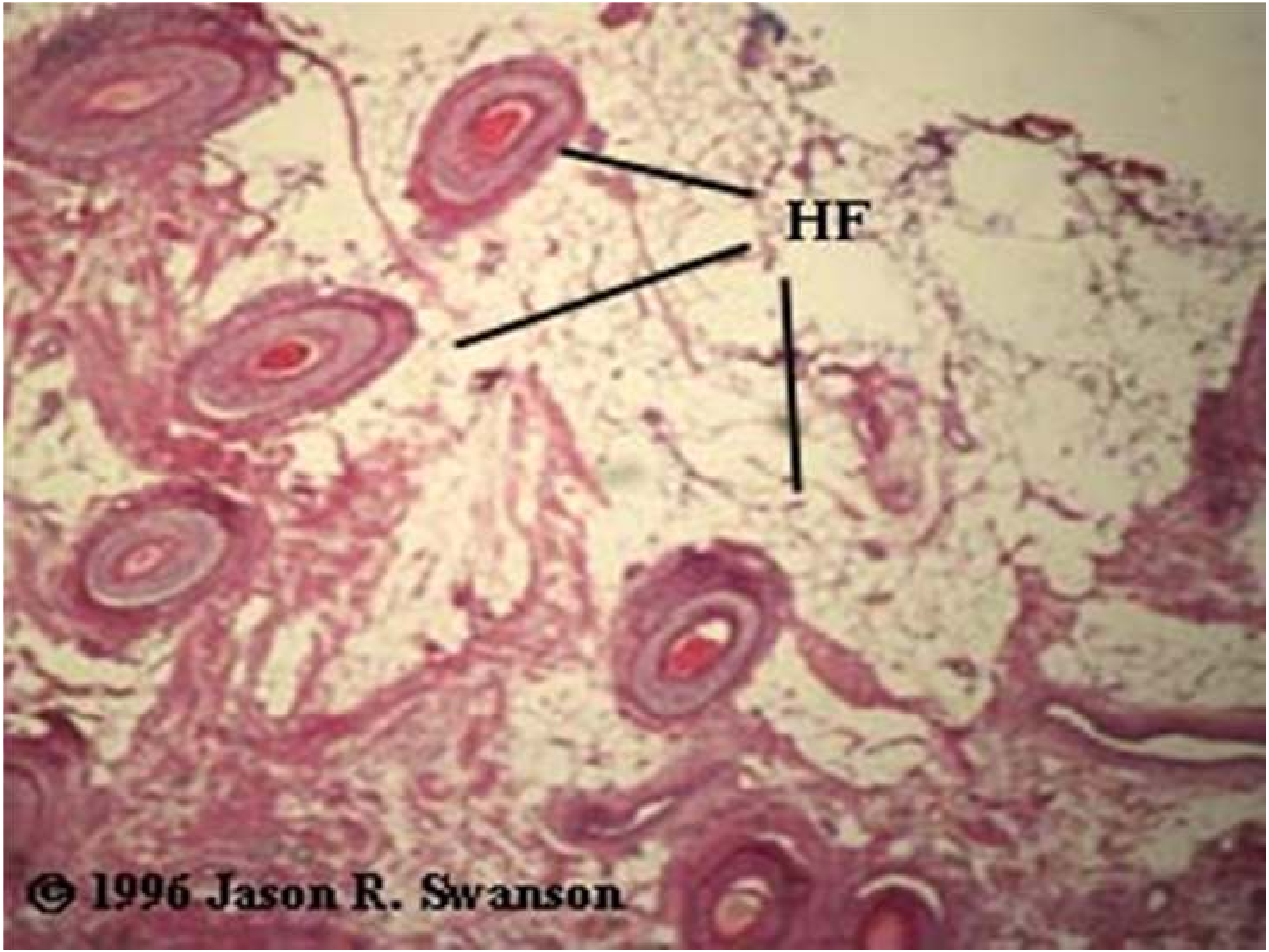


(a)



(b)

(c)


HF
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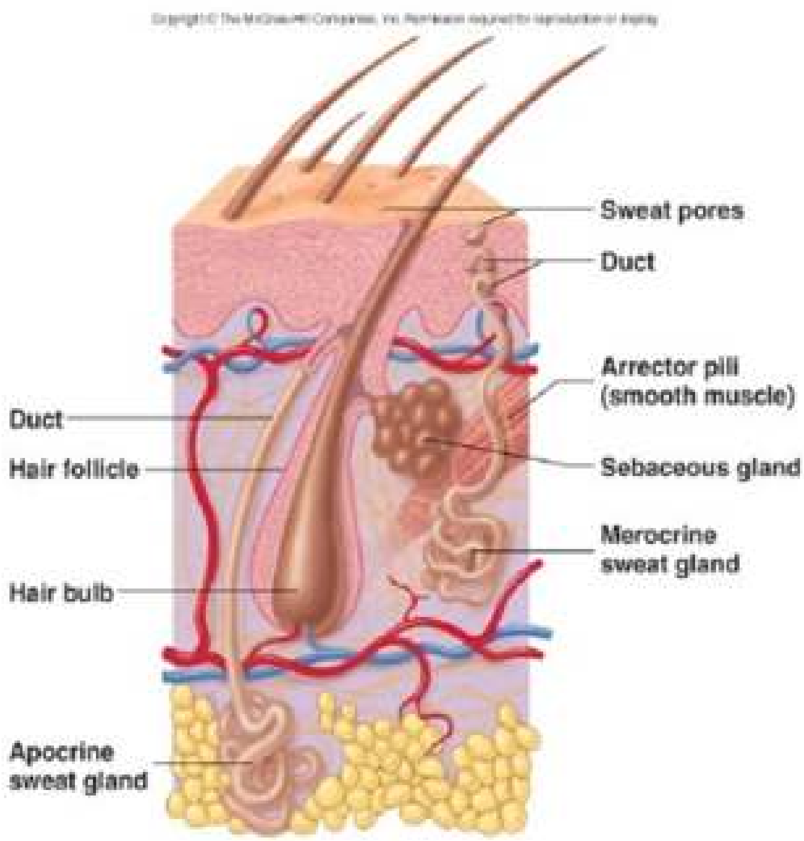
The sebaceous glands

- Are clusters of cells with a small dark nucleus and a foamy cytoplasm.
- They cluster around the hair shafts and their secretion is formed by total destruction of the cells, a mechanism called holocrine secretion.
- This secretion drains into the hair follicle and is discharged on the surface through the hair follicle opening.
- Sebaceous glands are seen in large numbers on the face, chest, and upper back.

Sebaceous (Oil) Glands



- Holocrine (death of secretory cells)
- Oily secretion (sebum)
  - Lanolin in skin creams is sheep sebum
- Prevents drying and may inhibit bacteria
- Most empty into hair follicle
  - Exceptions: lips, meibomian glands of eyelids, genitalia

Sudoriferous (Sweat) Glands

- Filtrate of plasma and some waste products
  - 500 ml of insensible perspiration/day
  - sweating with visible wetness is diaphoresis
- Two major types
  - **Merocrine**
  - **Apocrine**
- **Merocrine** or **eccrine**. Most common.
  - Simple coiled tubular glands.
  - Open directly onto surface of skin. Have own pores.
  - Coiled part in dermis, duct exiting through epidermis.
  - Numerous in palms and soles. Absent from margin of lips, labia minora, tips of penis, and clitoris.

The apocrine sweat glands

- Are found predominantly in the axilla, with a few seen also in the skin of the groin.
- They have a secretory component seen in the deeper dermis. The secretory section has a very wide lumen, and the cells lining this lumen will be seen to be composed of columnar epithelium which appears to form glandular secretion by a ‘nipping off’ of the tops of the cells, a process known as decapitation (holo-merocrine) secretion.
- The excretory channels of the apocrine glands most commonly drain into the canal of the hair shaft and sebum passes from here out on to the surface of the epidermis.

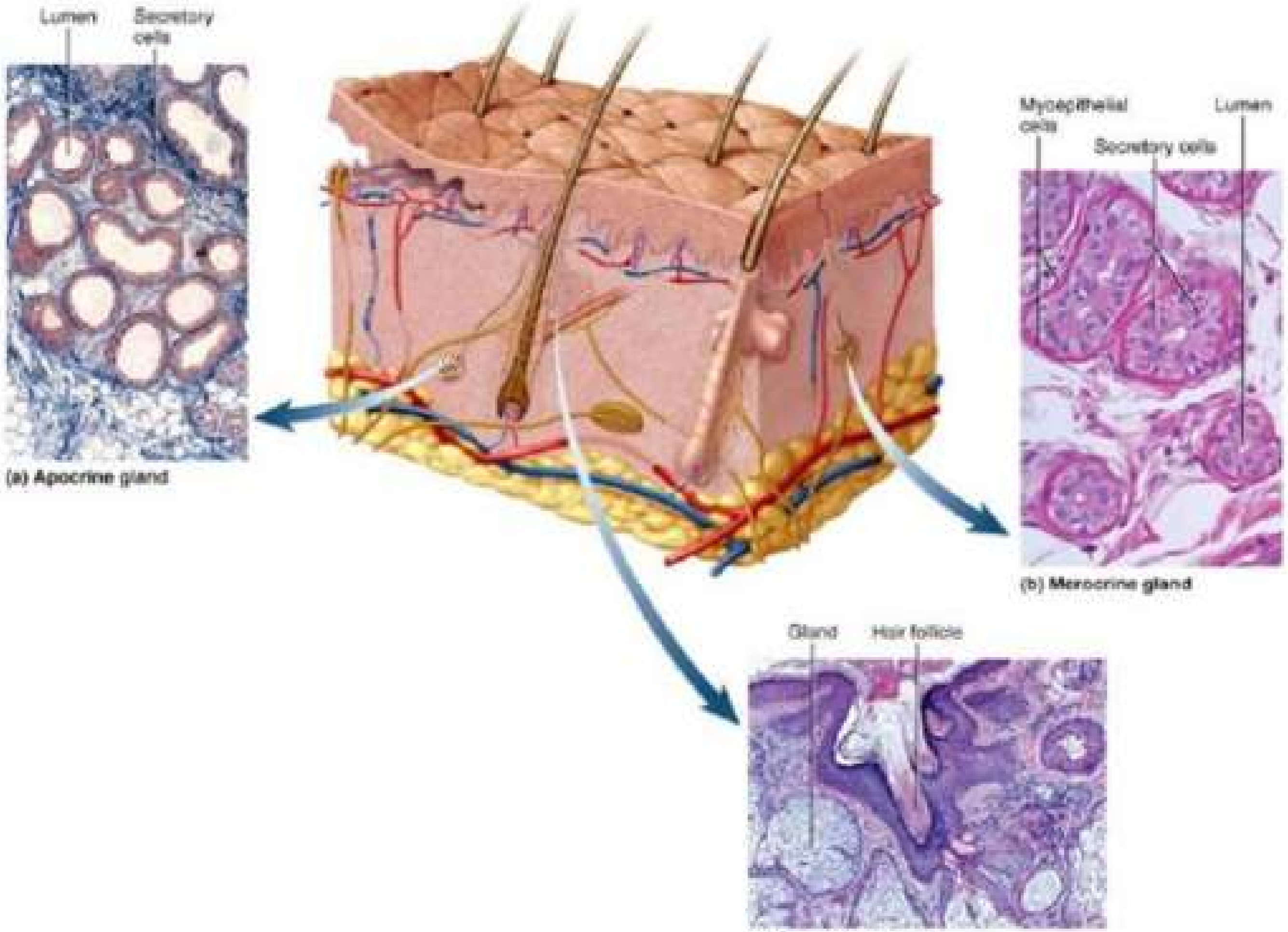
Sudoriferous (Oil) Glands

- Apocrine glands produce sweat containing fatty acids
  - Found only near hair follicles and respond to stress and sex
  - Secretion: organic compounds that are odorless but, when acted upon by bacteria, may become odiferous.
  - Found in axillae, genitalia (external labia, scrotum), around anus.
  - Bromhidrosis is body odor produced by bacterial action on fatty acids

The eccrine sweat glands

- Are seen at all body sites (excepting lips, nailbeds and glans penis) and are anatomically independent from the other appendages.
- Their secretory components are much smaller than those of the apocrine gland, with a smaller lumen. The excretory duct of these gland winds upward in a spiral pattern through the dermis and epidermis to the surface; type of secretion – merocrine without cell destruction.

Cutaneous Glands



(a) Apocrine gland

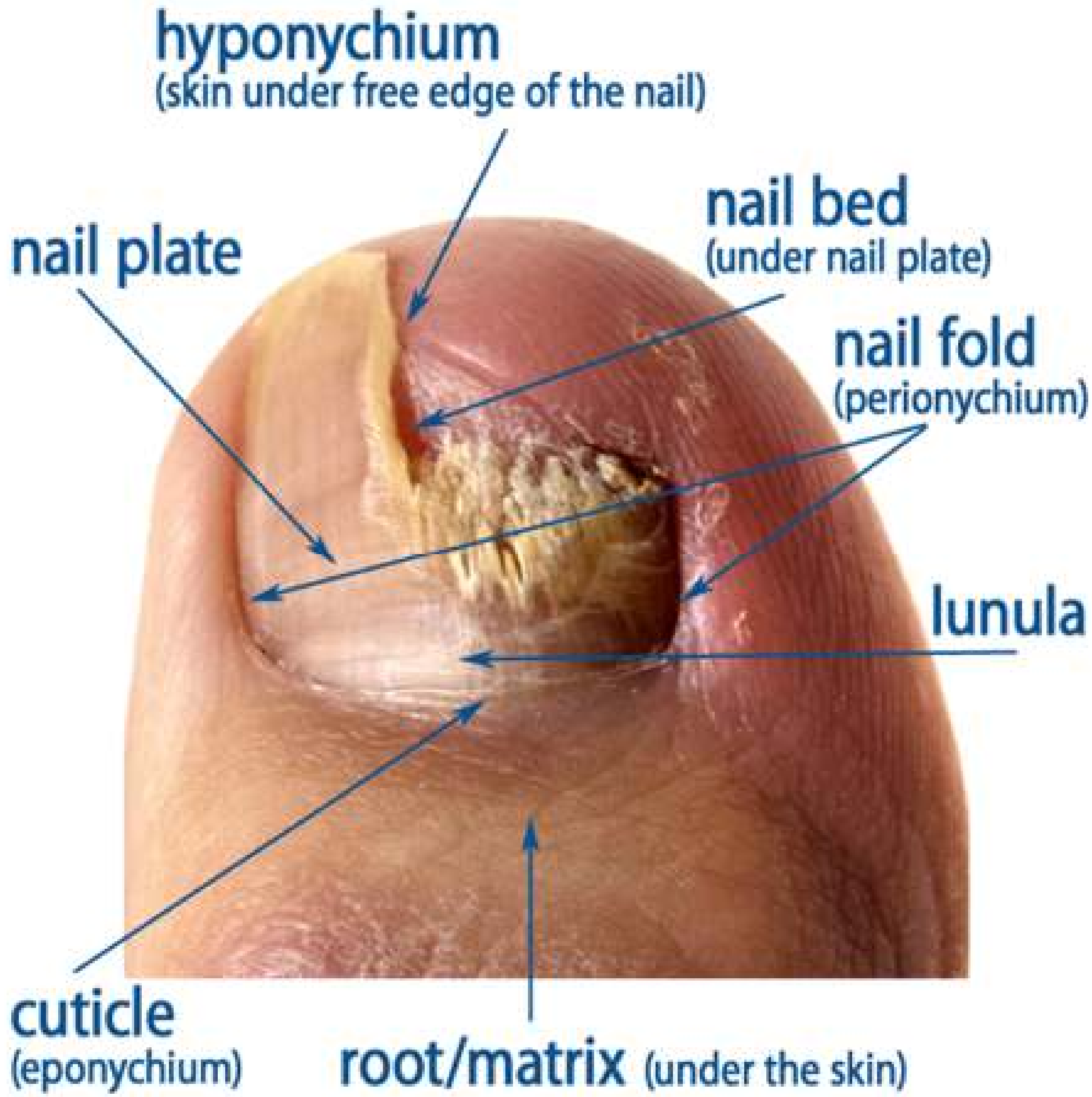
(b) Merocrine gland

(c) Sebaceous gland

The nails

- Are very highly modified skin appendages.
- The nail itself, or nail plate, grows out from the nail matrix and rests on the underlying nail bed.
- The pale halo at the proximal end of the nail is called the lunula, and around the edge of this there is a protective rim of cuticle.
- Nails may become involved in a number of skin diseases, such as psoriasis and fungal infection.
- The average time for a fingernail to grow out completely from base to outer edge is approximately 6 months, and for toenails the time is 6-18 months or even longer.

Nail anatomy



Functions of the Skin

- Protection against trauma, fluid loss, chemical attack, ultraviolet light, and infection
  - packed with keratin and linked by desmosomes
  - acid mantle (pH 4-6) - keep bacteria in check
- Excretion of salts, water, organic wastes
- Maintenance of normal body temperature through insulation or evaporative cooling, as needed
- Synthesis of vitamin D3; converted to calcitriol, a hormone important to maintaining Ca++ balance
- Sensory receptor - detects touch, pressure, pain, temperature stimuli
- Nonverbal communication - facial expressions

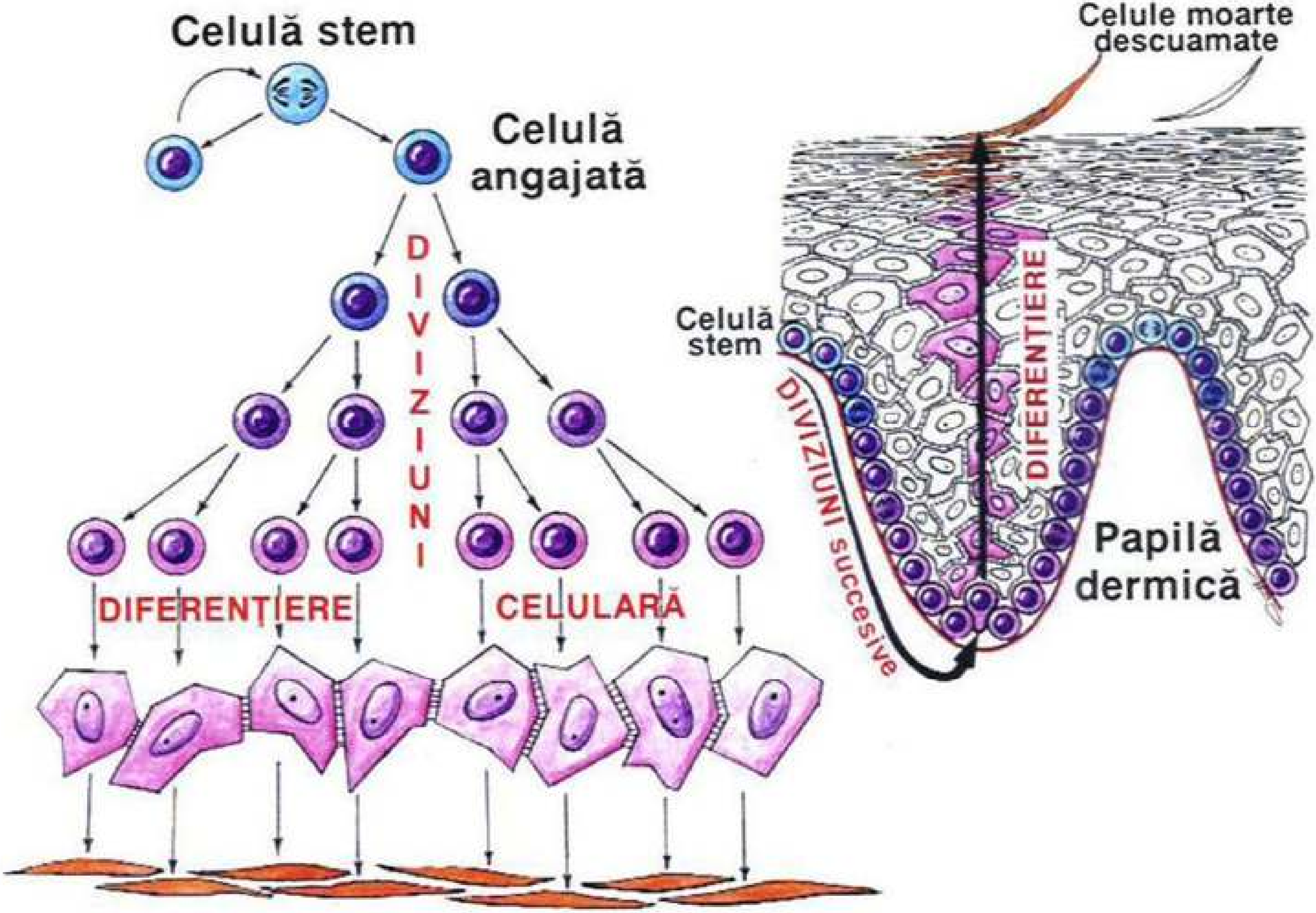
The skin functions

Two main functions of epidermis:

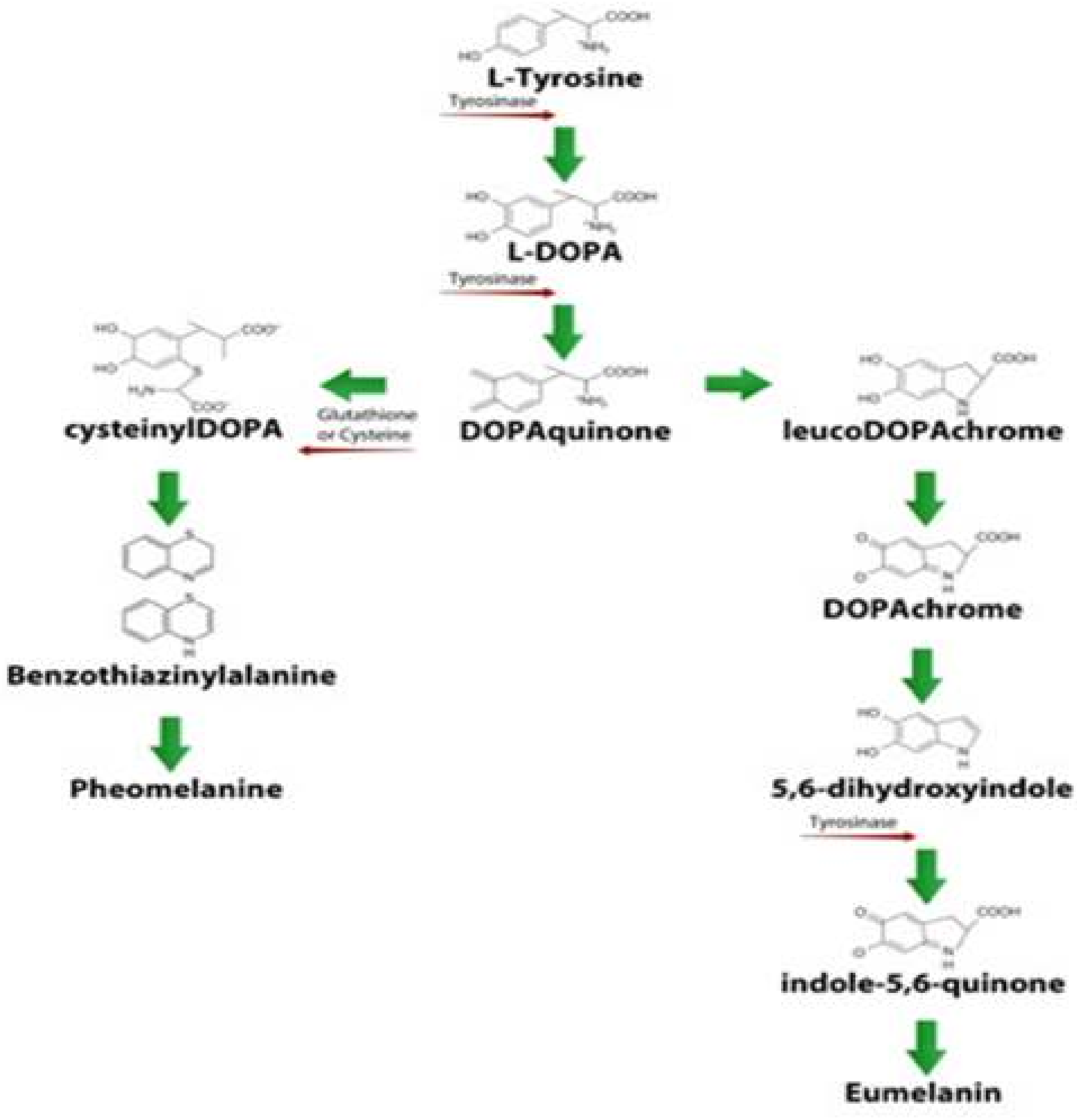
- keratin-genesis
- Melanin-genesis

Other three important functions of epidermis:

- barrier function (toxins, UV, etc.)
- prevention of desiccation
- immune surveillance (Langerhans cells)



Celulă stem
Celulă angajată
DIVIZIUNI
DIFERENȚIERE
CELULARĂ
Celule moarte descuamate
Celulă stem
DIFERENȚIERE
DIVIZIUNI succesive
Papilă dermică



L-Tyrosine
Tyrosinase
L-DOPA
Tyrosinase
cysteinylDOPA
Glutathione or Cysteine
DOPAquinone
leucoDOPAchrome
Benzothiazinylalanine
Pheomelanine
DOPAchrome
5,6-dihydroxyindole
Tyrosinase
indole-5,6-quinone
Eumelanin

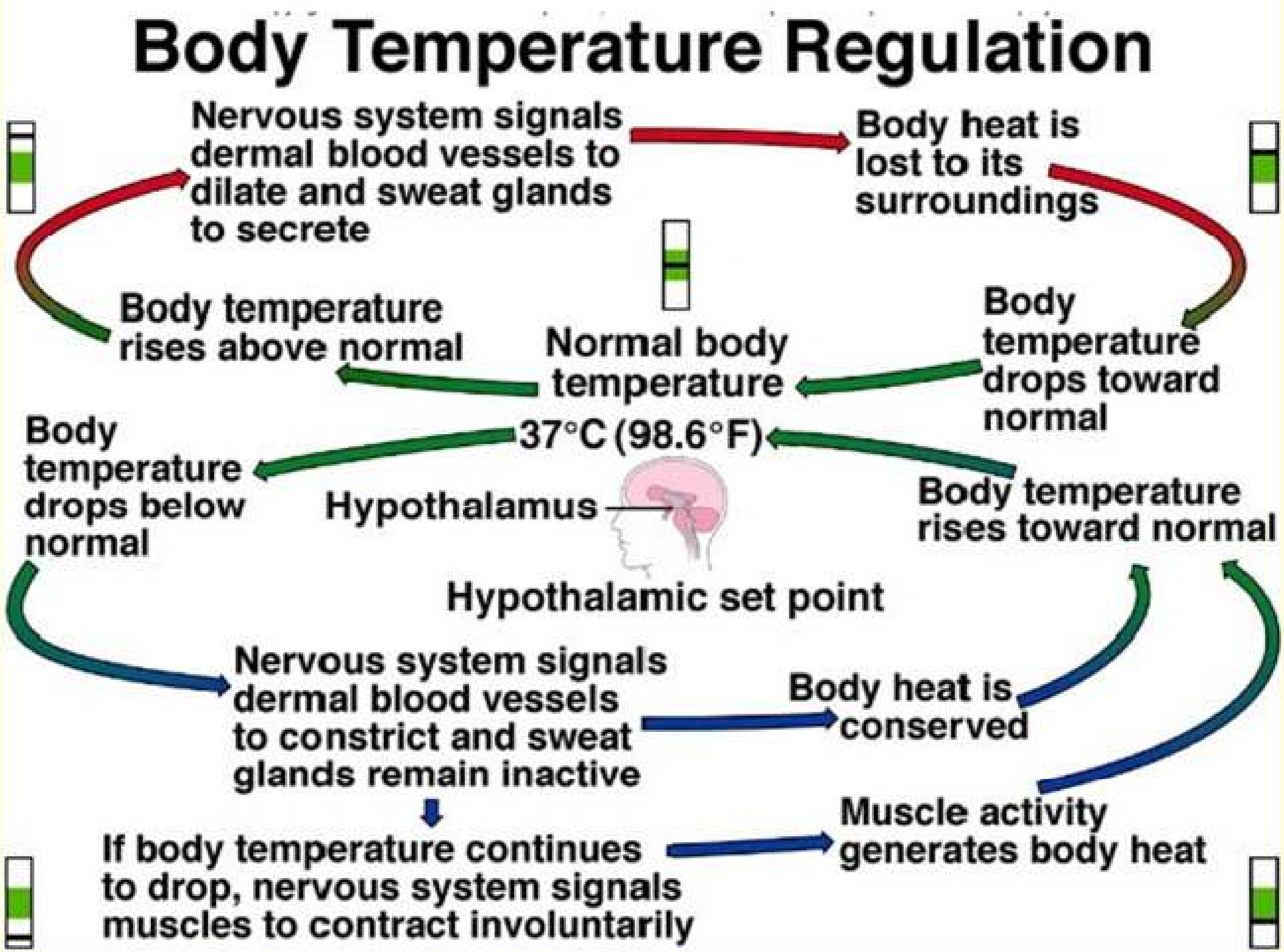
The skin functions

Two main functions of dermis:

- Temperature regulation through control of cutaneous blood flow and sweating, achieved by dermal vessels and eccrine sweat glands
- Mechanical protection of underlying structures, achieved primarily by the collagen and hyaluronic acid.

Three main functions of subcutis:

- Caloric reserve
- Heat insulator
- Shock absorber


Body Temperature Regulation
Nervous system signals dermal blood vessels to dilate and sweat glands to secrete
Body heat is lost to its surroundings
Body temperature rises above normal
Normal body temperature
37°C (98.6°F)
Body temperature drops toward normal
Body temperature drops below normal
Hypothalamus
Body temperature rises toward normal
Hypothalamic set point
Nervous system signals dermal blood vessels to constrict and sweat glands remain inactive
Body heat is conserved
If body temperature continues to drop, nervous system signals muscles to contract involuntarily
Muscle activity generates body heat
Figure 6.11

Skin physiology

- Basal cell replication rate: once every 200-400 hours.
- Trans-epidermal cycle time: about 28 days.
- Growth rate for scalp hair: 0.4 mm/24 h.
- Normal hair fall (scalp): 50-100/24 h.
- Fingernail growth: 0.1 mm/24 h (toenail is less).
- Skin blood flow is controlled by shunting arterio-venous anastomoses.
- Minimum insensitive perspiration: 0.5 1/24 h.

Skin biochemistry

- **Keratins** are made up of polypeptide helical coils linked by covalent bonds. They form the horny layer, nails and hair.
- **Melanin** is a complex polymer synthesized from tyrosine. There are eu- and phaeo-types; melanins absorb free radicals and energy including UV.
- **Collagen** is a polypeptide polymer which comprises 75% of the dry weight of the dermis. It is synthesized by fibroblasts.
- **GAG** makes up the ground substance of skin. They provide viscosity and hydration, andean exist as high MW polymers.
- **Vitamin D:** cutaneous UV activation produces the active form vitamin D3 from the inactive 7-dehydrocholesterol via the precursor previtamin D3.
- **Androgen** receptors in hair/sebaceous glands make these structures sensitive to the androgen surge of puberty.