Histology of the Skin

Dr. Mustafa Saad (2021)
The Skin

- The skin is the largest organ in the body, accounting for about 20% of total body weight with a surface area of about 2m².

- Also called the *cutaneous layer* and *integument*, it’s the boundary between the internal and external environment of the body.

- It’s formed of the epidermis and dermis. A fatty layer called the hypodermis (subcutaneous layer) connects the skin to the underlying tissues. Other structures found in the skin include:
  - Sensory organs
  - Arrector pili muscle
  - Hair
  - Nail
  - Sebaceous and sweat gland
  - Mammary glands

Epidermal derivatives
Fig. 1: The skin.
Functions of the skin

1) **Protective function:**
   - Physical barrier against thermal and mechanical stresses and against harmful substances.
   - Protection against microorganisms.
   - Protection against ultraviolet light.
   - Prevent the excessive loss of water through the skin.

Skin has a lipid-rich layer making it a selectively permeable membrane. It allows the passage of lipophilic substance (like drugs) through the skin, but prevents water loss. This has permitted life to be terrestrial. Without this function of the skin, the organism must spend a lot of time submerged in water.

*What is the first step in the treatment of extensive burns?*
2) **Sensory function:**
- Mechanical, thermal, pain.

3) **Thermoregulatory function:**
- Insulation.
- Sweating.
- Superficial microvasculature.

4) **Metabolic function:**
- Synthesis of vitamin D$_3$ through the action of UV light.
- Excretion of excess electrolytes with the sweat.
- Storage of energy as fat in the subcutaneous layer.
The Epidermis

- **Stratified squamous keratinized epithelium** formed mainly of epithelial cell called *keratinocytes* arranged in strata (layers) and connected with each other by desmosomes.

- Other cells found in the epidermis are *melanocytes*, *Merkel cells*, and *Langerhans cells*.

- Histologically, the skin can be classified into *thin* and *thick* skin *according to the thickness of the epidermis*. In the palms and soles we have thick skin with a much thicker epidermis formed of 5 strata; elsewhere, we have thin skin with a thinner epidermis formed of only 4 strata.

- Total skin thickness, however, is the thickness of both the epidermis and dermis. It’s thickest on the back and thinnest on the eyelids.
Fig. 2: The epidermis.
The layers of the epidermis

i. *Stratum basale*
- The deepest layer lying directly on the basal lamina.
- Formed of a single layer of basophilic cuboidal cells.
- Cells are connected to basal lamina by hemidesmosomes and to adjacent keratinocytes in the stratum basale and spinosum by desmosomes.
- The cells are highly mitotic and are the progenitor cells of all epidermal layers. As these keratinocytes mature they migrate upwards (superficially) until they reach the surface where they are shed. Renewal of the epidermis takes about 15-30 days.
- A characteristic intermediate filament called *keratin* is found in all keratinocytes.
ii. **Stratum spinosum**

- The thickest epidermal layer. It’s thickest in thick skin.
- Formed of polyhedral cells active in keratin synthesis.
- The cells close to the stratum basale are also mitotically active and together they’re called the *stratum germinativum*.
- Keratin filaments become thick tonofibrils attached to desmosomes. When the tissue is prepared, the cells shrink and these desmosomes and tonofibrils appear as spines on the surface of the cell, hence the name.

Fig.3: The spines of the stratum spinosum. Left, light microscope. Right, electron microscope. Note the tonofibrils attached to the desmosomes.
### iii. *Stratum granulosum*

- Formed of 3-5 layers of cells.
- Cells contain two types of granules:

<table>
<thead>
<tr>
<th>Keratohyaline Granules</th>
<th>Lamellar Granules</th>
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<tbody>
<tr>
<td>Contain keratin tonofilaments associated with proteins</td>
<td>Contain various lipids</td>
</tr>
<tr>
<td>Non-membranous</td>
<td>Membranous</td>
</tr>
<tr>
<td>Contents remain in cell</td>
<td>Contents are released to the outside of the cell</td>
</tr>
<tr>
<td>Appear as basophilic structures under the light microscope</td>
<td>Seen as oval structures with several lamellae under the electron microscope</td>
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○ The lipids of the lamellar granules are released to the outside by exocytosis filling the intercellular space with lipid. This creates a hydrophobic barrier that prevents water loss.

Fig.4: The lamellar granules of the stratum granulosum and the lipid-rich intercellular barrier.

iv. **Stratum lucidum**
○ A translucent layer found only in thick skin.
○ Formed of eosinophilic squamous cells with no nuclei and organelles.
○ Cytoplasm filled with keratin.
v. **Stratum corneum**
- Most superficial layer. Thicker in thick skin.
- Formed of 15-20 layers of thin squamous cells which are called *squames*. These are nothing more than cell membranes filled with keratin.
- The cells of the deeper layers of the stratum corneum are surrounded by the lipid-rich barrier and the most superficial cells are continuously shed.

Calluses are areas of thickened stratum corneum due to repeated friction. (you may already have one in your middle finger from excessive use of pens/pencils).
Other cells of the epidermis

Melanocytes

- Neural crest derived cells found in the stratum basale and the hair follicle and produce the dark (or red) pigment melanin.
- The pale-staining cell body is found between the keratinocytes of the stratum basale but is not attached to them. The cell body, however, is attached to the basal lamina by hemidesmosomes.
- The cytoplasm contains mitochondria, rough endoplasmic reticulum, and Golgi apparatus. Several processes extend between the cells of the stratum basale and spinosum.
- Melanin inside melanocytes is stored in granules called melanosomes. These are transported to the processes. The tips of these processes are engulfed by keratinocytes and the melanosomes form a supranuclear cap to protect DNA from the harmful effects of UV light.
O Although produced by melanocytes, there’s more melanin in keratinocytes than in melanocytes.

O A melanocyte and its associated keratinocytes are called an **epidermal-melanin unit**. The density of these units is the same in all individuals. It’s the rate and amount of production that differs.

**Color of the skin is the result of several factors, the most important are** (1) melanin pigment, (2) carotene pigment, and (3) blood in the vessels.

**Fig.5:** Melanocytes. Note how the cell body is found within the stratum basale (SB) and the processes extend into the stratum spinosum.
Langerhans cells
- Antigen-presenting cells found mainly in the stratum spinosum with processes extending between keratinocytes of all the layers.
- They bind and present antigens to lymphocytes, thus playing an important immune role.

Merkel cells
- Mechanoreceptors for light touch. Most abundant in fingertips.
- Found between the cells of the stratum basale. Cell body and processes attached to adjacent cells by desmosomes.
- Cytoplasm contains neurosecretory granules.
- Basal surface in contact with an expanded terminal of an unmyelinated nerve fiber.
A basement membrane is found between the epidermis and dermis. Hemidesmosomes attach the stratum basale of the epidermis to this membrane and collagen anchoring fibrils attach the dermis to it.

The surface of the dermis in contact with the epidermis is irregular with several dermal projections (dermal papillae) interdigitating with projections of the epidermis (epidermal ridges).

This interdigitation is very prominent in thick skin that it shows on the surface of the skin as a pattern of grooves and ridges which are the basis of fingerprints.

Fig.6: The dermal-epidermal junction.
✓ Importance of the jigsaw-like epidermal ridges-dermal papillae arrangement:

1. Increase surface area of contact between epidermis and dermis reinforcing the junction between them.
2. Increase the number of Merkel cells and Meissner corpuscles increasing tactile sensitivity.
3. Reflection of this pattern on the surface increases the surface area of the grip of the hand or foot by increasing friction.
4. The ducts of sweat glands open on the tops of the surface epidermal ridges as sweat pores. The sweat and ridges form fingerprints (or footprints) when a smooth object is touched. Since the pattern of the ridges is genetically determined, this can be used to identify an individual.
The Dermis

- A connective tissue layer found under the epidermis.
- Variable in thickness. Thickest on the back.
- Formed of two sublayers with indistinct boundary.

i. **Papillary region:**

- Thin superficial part of the dermis corresponding to the dermal papillae.
- Formed of loose areolar connective tissue.
- Contains:
  - Blood capillary loops
  - Lymphatic vessels
  - Nerves
  - Meissner’s corpuscles (of touch)
ii. **Reticular region:**
- Thicker deep part of the dermis.
- Formed of dense collagenous irregular connective tissue.
- Contains:
  - Collagen and elastic fibers
  - Lymphatic and blood vessel plexuses
  - Sensory receptors and nerves
  - Hair follicles
  - Arrector pili muscle
  - Glands

Fig. 9: Reticular region of the dermis.
In certain regions of the body, collagen fibers within the reticular region of the dermis tend to orient more in one direction than another because of natural tension resulting from bony projections, orientation of muscles, and movements at joints. Surgical incisions made parallel to these tension lines are associated with faster healing and less scarring.

Fig. 10: Tension lines.
Vascular plexuses of the dermis

- Two plexuses are found in the dermis:
  - *Subpapillary plexus* located between the papillary and reticular regions of the dermis. From it arise capillary loops that pass into the dermal papillae to supply nutrients to the epidermis.
  - *Deep dermal plexus* located deeper in the dermis.

- Anastomoses between the two plexuses are found and are important for the thermoregulatory function of the skin:
  - In cold conditions, blood flow to the subpapillary plexus is reduced to decrease heat loss.
  - In hot conditions, blood flow to the subpapillary plexus is increased to facilitate heat loss.

- Lymphatic vessels begin in the dermal papillae and then form two plexuses located with the blood vessels.
Fig. 11: Vascular plexuses of the skin.
Nerve Supply and Sensory Receptors

- Afferent sensory nerves enter the skin and end at epithelial and dermal receptors.
- Sweat glands, the arrector pili muscle, and blood vessels are supplied by postganglionic sympathetic nerves.
- No parasympathetic nerves supply the skin.

- Due to its large surface area and external location, the skin functions as a receiver of various stimuli from the environment.
- Various sensory receptors are found in the skin. Some have glial and collagenous covering and some are unencapsulated.
Fig. 12: Sensory receptors of the skin.
Unencapsulated receptors

- These are not covered by a glial or collagenous capsule.

- They include:
  1. **Tactile discs** associated with the epidermal tactile (Merkel) cells, which function as receptors for light touch.
  2. **Free nerve endings** in the papillary dermis and extending into lower epidermal layers, which respond to temperature, pain, and itching.
  3. **Root hair plexuses**, a web of sensory fibers surrounding the bases of hair follicles in the reticular dermis that detects movements of the hairs.
Encapsulated receptors

**Meissner corpuscles**

- Elliptical structure located in the dermal papillae perpendicular to the epidermis.
- Formed of:
  - Fibrous capsule
  - Several flattened Schwann cells arranged as lamellae
  - Unmyelinated nerve ending that winds among the Schwann cells until it reaches the tip of the receptor
- Responsible for the sensation of **light touch**.
- Most numerous in the fingertips, palms, and soles.

Fig.13: A Meissner’s corpuscle in dermal papilla.
**Lamellated (Pacinian) corpuscles**

- Large oval structures located deep in the reticular dermis and hypodermis.
- Formed of:
  - Fibrous capsule
  - Several concentric layers of flattened Schwann cells surrounded by layers of connective tissue
    - Sensory axon in the center
- Responsible for the sensation of **deep touch, pressure, and vibration**.
- May be found in other organs.

Fig. 14: Pacinian corpuscle.
Ruffini corpuscles
- Elongated fusiform structures found in the dermis.
- Formed of:
  - Thin capsule attached to surrounding tissue
  - Fluid-filled interior
  - Unmyelinated axon that branches profusely inside the capsule
- Respond to stretch.

Krause end bulbs
- Ovoid structures with extremely thin capsule.
- Found in skin of penis and clitoris, several mucous membranes, and in the epineurium of nerves
- Respond to vibration.
The Subcutaneous layer (hypodermis)

- Loose connective tissue layer that binds skin to underlying tissues.
- It contains adipocytes and a vascular plexus.

Functions:
- Enables the skin to slide over underlying structures
- Fat in this layer acts as an energy storage site, insulator, and shock absorber
- The rich vasculature enables rapid intake of drugs injected into this layer
The Hair

- Hairs are elongated keratinized structures derived from epidermal invaginations.
- Found throughout the body, except in certain areas like the palms, soles, lips, glans penis, clitoris, and the labia minora.
- Hair distribution differs according to genetic factors, gender, and region of the body.

Functions:
- Protection (Hair on head protects scalp, eyelashes and eyebrows protect eye).
- Reduction of heat loss.
- Sensation of light touch.
Parts of the hair

- **The shaft**: the superficial part of the hair that extends beyond the surface of the skin.
- **The Root**: the deeper part of the hair that reaches down into the dermis. It’s surrounded by the hair follicle.

- The hair is formed of 3 concentric layers:
  1. **The medulla**: The innermost layer of large, vacuolated cells.
  2. **The cortex**: The middle layer of cuboidal cells.
  3. **The cuticle**: The outermost layer. Formed of heavily keratinized squamous cells arranged like shingles on house roofs.

Fig.17:Layers of hair.
The hair follicle

- A downward extension of the epidermis that surrounds the hair root.

- Formed of (from the inside out):
  1. *Epithelial root sheath* derived from the epidermis and formed of two layers: (a) *internal root sheath* that disappears above the level of the attached sebaceous gland and (b) *external root sheath* that extends to the epidermis to become continuous with the stratum basale and spinosum.
  2. *Glassy membrane*: the thickened basement membrane that separates the epithelial and dermal root sheaths.
  3. *Dermal root sheath* derived from the connective tissue of the dermis.
The lower part of the hair follicle is expanded to form the *hair bulb*. This hair bulb:

- Is invaginated by the *hair dermal papilla* which contains loose areolar connective tissue and blood vessels that nourish the hair.
- Contains the *hair matrix* formed of keratinocytes continuous with the stratum basale of the epidermis. The matrix is responsible for the formation of the hair. Within the hair matrix, we have melanocytes that give hair its color.
- Is surrounded by the hair root plexus.
Fig. 18: The hair follicle. To the right, the expanded part is the hair bulb. Above, a cross section through the hair follicle.
The *arrector pili* muscle is a bundle of smooth muscle cells that extend from the superficial part of the dermis to the dermal sheath of the hair follicle. Under stressful conditions (cold), the muscle contracts pulling the hair so that the shaft becomes perpendicular to the surface and bulging the skin around the hair producing ‘goosebumps’.

Fig. 19: Action of the arrector pili muscle.
Hair growth

- Hair growth is cyclical. However, it’s asynchronous and occur at different rates in different regions of the body (even in the same region).

- Phases of hair growth:
  1. **Anagen**: a generally long period of mitotic activity and growth.
  2. **Catagen**: a brief period of arrested growth and regression of the hair bulb.
  3. **Telogen**: a long period of inactivity in which the hair may be shed.

Fig. 20: Phases of hair growth.
Sebaceous Glands

- Simple branched acinar holocrine glands.
- Found in the angle between the arrector pili muscle and the hair follicle. With the hair follicle, it forms the *pilosebaceous unit* derived from the same stem cells.

- Found in most regions of the body with highest density in the face and scalp. They are absent in the palms and soles.
- Duct opens into hair follicle. In hairless regions (eyelids, nipples, penis, and clitoris), the duct opens directly onto the epidermal surface.

- Secretion of these glands is called *sebum* and it’s mainly formed of lipids. The cells that produce it are called *sebocytes*.
- Sebum helps maintain the stratum corneum and the hair shaft and has some antibacterial effect.
Fig. 21: (a) The pilosebaceous unit and the arrector pili muscle. (b) Histological appearance of the sebaceous gland. Note the capsule (C) and white appearance of the sebocytes (S).
Acne vulgaris is an inflammatory disorder of the pilosebaceous unit in which there is excessive keratinization and sebum production that leads to blockage of the duct of the gland. This will lead to accumulation of sebum that may be infected. It most commonly occurs during adolescence.

Demodex folliculorum is a small mite that normally lives in the hair follicle and feeds on dead cells and sebum. It’s thought to be implicated in some skin disorders, but nothing is conclusive yet.
Sweat Glands

- Long epidermal invagination. They are simple coiled merocrine glands of two types:

  1. **Eccrine sweat glands**
     - Found all over the body with highest density in palms and soles.
     - Play an important role in thermoregulation with some excretory function.
     - Controlled by the sympathetic nervous system and function from birth.
     - The secretory portion has a small lumen with stratified arrangement of cells. The coiled duct is lined by two layers of more eosinophilic epithelial cells filled with mitochondria. These duct cells absorb Na\(^+\) ions to prevent excessive loss of this electrolyte. They open on the surface of the skin at sweat pores.
Cells of the secretory portion are:

1. **Clear cells:** Pale staining with numerous mitochondria. Microvilli and basal infoldings increase the surface area. They do not reach the lumen. Interstitial fluid from nearby dermis is taken up by these cells and released into intercellular canaliculi. They secrete the water and electrolytes components of sweat.

2. **Dark cells:** Inverted-cone-shaped cells. They reach the lumen but do not rest on the basal lamina. The cytoplasm contains mitochondria, Golgi apparatus, and rough endoplasmic reticulum. The wide apical part is filled with strongly eosinophilic granules. They release glycoproteins by exocytosis into the lumen.

3. **Myoepithelial cells:** Rest on the basal lamina. They contract to help push sweat into the ducts.
Fig. 22: (a) Eccrine sweat gland. Note its opening. (b) The types of cells in eccrine sweat glands secretory portion.
i. **Apocrine sweat glands**
- Found in the axillary and perianal regions.
- Controlled by the sympathetic nervous system and sex hormones. They become fully functional after puberty.
- The secretory portion has a large lumen with simple cuboidal eosinophilic cells. The duct opens into the hair follicle near the epidermis.
- They produce a viscous protein-rich secretion. In humans, they may also produce pheromones but in a reduced manner.
- The secretion of these glands is odorless. Bacteria act on this secretion giving it a distinctive odor; this is what is called ‘**body odor**’.

*Note:* When first discovered, these glands were thought to be apocrine and were named so. Research, however, have shown that they actually release their secretions by exocytosis and, thus, were merocrine glands.
Fig. 23: (a) Apocrine sweat gland. Note its opening. (b) Secretory portion of eccrine sweat gland with a small lumen. D = duct. (c) Secretory portion of apocrine sweat gland with a larger lumen.
<table>
<thead>
<tr>
<th>Feature</th>
<th>Eccrine</th>
<th>Apocrine</th>
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<tbody>
<tr>
<td>Location</td>
<td>All over the body, especially palms and soles</td>
<td>Axillary and perianal regions</td>
</tr>
<tr>
<td>Type</td>
<td>Simple coiled</td>
<td>Simple coiled</td>
</tr>
<tr>
<td>Secretion</td>
<td>Watery</td>
<td>More viscous</td>
</tr>
<tr>
<td>Method of secretion</td>
<td>Merocrine</td>
<td>Merocrine</td>
</tr>
<tr>
<td>Secretory portion</td>
<td>Small lumen. Stratified epithelium</td>
<td>Large lumen. Simple epithelium</td>
</tr>
<tr>
<td>Open</td>
<td>Usually on the surface of the skin</td>
<td>Into the hair follicle</td>
</tr>
<tr>
<td>Control</td>
<td>Nervous (cholinergic)</td>
<td>Nervous (adrenergic) + Hormonal</td>
</tr>
<tr>
<td>Onset of action</td>
<td>From birth</td>
<td>At puberty</td>
</tr>
<tr>
<td>Functions</td>
<td>Thermoregulation, Excretion</td>
<td>Stimulated during emotional stress</td>
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Nails

- Hard plates of keratinized cells found on the dorsal surface of the distal phalanges.

- Externally, the nail is formed of a nail plate (body) surrounded by three folds (two lateral and one proximal) with a distal free edge.

- The proximal part of the nail is the *nail root* which is covered by the proximal nail fold. At this fold, the stratum corneum doesn’t pass with the other layers of the epidermis but continues distally as the *eponychium* (cuticle).

Fig. 24: External appearance of nails.
The nail root is formed from the *nail matrix* derived from the epidermis. As more cells are added, the root grows and the plate extends distally over the *nail bed*.

Proximally in the nail plate, we have a whitish area called the *lunula*. The white color comes from the opaque nail matrix under the lunula. The nail bed is thin formed of stratum basale and spinosum only. Because of this and because the mature nail plate is semitransparent, the color of blood in the dermal vessels is seen through the nail.

Distally, the free edge of the nail is adhered to the fingertip by a fold of epidermis called the *hyponychium*. 
Fingernails grow at a faster rate than toenails. This is why we clip fingernails more often.

Fig. 25: Histology of the nail.
Thank You