MUSCULOSKELETAL SYSTEM

< EPIDERMIS & DERMIS > < PART 1 >

DONE BY:
RENAD ABURUMAN & RAMA AWAMLEH

*this sheet contain slides & what doctor said(*) without picture.
• The organs of the **integumentary system** include the skin and its accessory structures including hair, nails, and glands, as well as blood vessels, muscles and nerves.

• **Dermatology** is the medical specialty for the diagnosis and treatment of disorders of the integumentary system.

  **Structure of the Skin**

• The skin (**cutaneous membrane**) covers the body and is **the largest organ** of the body by surface area and weight

• Its area is about **2 square meters** (22 square feet) and weighs **4.5-5kg** (10-11 lb), about 16% of body weight

• It is **0.5 – 4 mm thick**, thinnest on the eyelids, thickest on the heels; the average thickness is **1 – 2 mm**

  *The doctor mention the **bold** numbers.

  **Skin Layers**

1) Epidermis and derivatives – (ectoderm):

*All structure that have epithelial, the origin of them will be from **ectoderm**.

*epithelial tissue of skin.

   a) Epidermis proper    b) Hair follicles    c) Nails

   d) Glands ➔ Sebaceous, sweat (eccrine & apocrine), Mammary
2) Dermis – Corium (mesoderm): *CT part of skin
   
   a) Papillary layer – loose CT → more cell.
   
   b) Reticular layer – dense Ct → more fiber.

- Subcutaneous (hypodermis) subcutis (mesoderm):
  * not a layer of skin.
  - Areolar CT
  - same as superficial fascia.
  - Fatty components

Functions of Skin

- Major functions of skin
  - Protection
  - Thermoregulation
  - Excretion
  - Secretion
  - Sensory reception – communication
  - Immunoprotection – there are more lymphocytes in the skin than in circulation

- Problems of burn victims exemplify the importance of skin.
- Patients with severe burns has:
  1. Loss of sensation to temperature (not only temp. but to everything)
  2. Pain and pressure
  3. Ionic balance drastically off
  4. Fluid loss (by a lot of edema occurring)

* point 3&4 mean loss of hemostasis → may lead to death
5-Wildly fluctuating body temperature (*5-8 degrees) → because of damage of blood plexus that regulate temp.

6-Bacterial and fungal infections increase (*because it’s the protection organ in the body).

**Epidermis**

- Most superficial layer of skin.
- Cornified (keratinized) stratified squamous epithelium. → *this type of tissue only present in the skin, oral cavity and the end of anal canal.
- Two major types of skin based on thickness of epidermis:
  1) **Thick skin** on non hairy (no hair follicles) surfaces (epithelium up to 1.0 mm)
  2) **Thin skin** on most hairy surfaces of the body (epithelium generally 0.1 mm)
- Thick vs thin does not reflect true thickness of skin including dermis.
- Skin on the back called thin but actually is thickest when dermal layer is included.
Cells of Epidermis

- Four cell types in the epidermis:

  1) **Keratinocytes** (squames): production of keratin and water barrier. More than 90% of cells in epidermis.
    *basic of epidermis.*

  2) **Melanocytes** – pigment production less than 5% of cells in epidermis.
    *protection against UV light by melanin.*

  3) **Langerhans cells** (زبال الجلد) – immune response, 1-3% cells in epidermis.
    *come from bone marrow.*
    *almost it is the macrophages of skin.

  4) **Merkel cells** – sensory reception and local endocrine control, 1-3% cells of epidermis.
    *have connection with nerve ending.*

- Differentiation of keratinocytes (cytomorphosis):
  
  1) Change shape (flatten)
  *cuboid → polyhedral → sequumus (flatt in shape)
  2) Lose organelles (*to become dead cell).
  3) Form fibrous proteins
  4) Become dehydrated (*cytoplasm disappear*).
  5) Produce products that thicken plasma membranes (*contribute in water proof*).
    *the differentiation start from St. Basale and continue to st. cornium*.
Layers (Strata) of the Epidermis:

*from superficial to deep .

1) Stratum corneum
2) Stratum lucidum
3) Stratum granulosum
4) Stratum spinosum
5) Stratum basale

Stratum Basale (Germinativum)

*have only one layer

- The **mitotically active** *(because it have stem sells)* layer which generate the keratinocytes and their derivatives (i.e. Merkel cells)
- Cells anchored to basal lamina (basement membrane) via anchoring fibrils and **hemidesmosomes** *(only layer have it)*.
- Highest metabolic requirement of all layers
- Active synthesis of tonofilament, formation of extensive number of **desmosomes**

* هي الأساس الذي نتمركز عليه في تكوين الكيراتين وهي جزء: **tonofilaments** • من .cytoskeleton

- Cells assume **cuboid** profiles
- Two major cell types:
  - Stem cells → stay fixed
  - Keratinocytes→ascending to upper layer.
- This layer contain the most undifferentiated cells of epidermis

*tonofilments → tonofibrils → keratin fibers.*
Stratum Spinosum

* have spine-like structure after preparation under microscope.
* 3 to 4 layers.

- **Polyhedral** cells
- Cells are firmly bound by the filament-filled cytoplasmic spines and desmosomes
- Active synthesis of tonofilaments which provides cytoskeletal framework
  - Tonofilaments insert into the cytoplasmic part of the desmosomes
- Appearance of **membrane-coated granule (MCG)** (laminal granule is the right name) in upper portion of this layer
  - These are laminated structures (plates in shape)
  - Key to formation of **effective water barrier** (*in this layer there is no function, later on after the release of it in upper layer it will become water proof)
  - MCG contain lamellar disks that are formed by **lipid bilayers** (look like cell membrane).

- **Mitotic figure** frequent (up to 3%)
  - All mitosis are confined to the **malpighian layer** (layers that have mitotic activity → both stratum basale and stratum spinosum)

Stratum Granulosum

- Presence of dense, refractile, basophilic **granules of keratohyalin** which contain **profilaggrin**.
- **granules of keratohyalin**: it’s the precursor to filaggrin, that when release from it become filaggrin, that connect between **tonofibrils** to produce **keratin fiber**.
- The basophilia is due to RNA within the **granules** (active sites of filaggrin synthesis)
• Tonofilaments have condensed into tonofibrils which are anchored in the matrix of the granules
• Many desmosomes present
• MCG are released into extracellular space
  – thicken external surface of membrane and seal adjacent membranes thus forming a water barrier (note no zonula occludens)

Stratum Lucidum
• Only in thickest skin (palms, soles)
• Appears as transparent layer, no visible nuclei or organelles (EPR).
• Sulfhydryl groups (-SH) replaced by disulfide bonds -strong bond-(S-S) thus forming cystine groups (bind between cysteine amino acid) that cross linked and stabilize the keratin molecules
• Substance remaining in these cells called eleidin:
  – Clear intracellular protein
  – Intermediary (مرحلة متوسطة) in formation of keratin from keratohyaline granules and tonofibrils.

Stratum Corneum
*flat filled cell with strong keratin fiber
• Plasma membranes thickened by previous emptying of MCG into intercellular space in the subjacent layer
• Desmosomes remain as membranous modifications
• All organelles lost
• Cells backed with keratin (tonofibrils embedded in matrix of keratohyalin)
• Cell structure not evident

*(tonofibril + filaggrin) by cystine group → strong keratin fiber
• **Stages of keratinocytes development:**
  1) Proliferation (occur in the Basale & the beginning of spinosum)
  2) Differentiation
  3) Exfoliation (disappear of cells \ regeneration)

  - Usually (28-45 days) 1-1.5 months for **complete cycle** (cells of epidermis change)

• Thin skin lacks (not) well developed:
  1) Stratum corneum
  2) Stratum lucidum (sometimes absent)
  3) Stratum granulosum

**Pigmentation system**

• Melanocytes (large cell).
  _Appear as clear (neuron-like) cells within st. Basale._
  
  - Do not form desmosomes with keratinocytes (because its not from the same origin)
  - Extend dendritic-like processes (arm process) throughout st. spinosum
  - Same number of melanocytes in all races
  - Main function → Produce melanin & Transfer melanin to keratinocytes *in apical part of it.*
  - Originate from **neural crest.**

• Tyrosinase catalyzes conversion of tyrosine to 3,4-dihydroxyphenyalanine (DOPA) and conversion of DOPA to dopaquinone which eventually forms melanin (الدكتور حكا أنو مالاننا بهاي لا أنها بيوكم)

• Stages of melanocyte **melanogenesis** (melanization of the melanosome; a membrane-limited body derived from Golgi apparatus):
  1) Premelanosome (Golgi apparatuses):
    - **Circular** vesicle
    - **High** Tyrosinase activity
    - Fine peripheral granules
2) Immature melanosome:
   - **Ovoid** vesicle
   - Tyrosinase activity
   - Parallel filaments 10 nm periodicity

3) Mature melanosome:
   - **Internal** structure obscured by melanin
   - Tyrosinase activity still present but low.

4) Melanin granule:
   * appear in appendages (arms)
   - **Solid** melanin
   - **No** tyrosinase activity

- Transfer of melanin from melanocyte to keratinocytes is by a process termed “Cytocrine secretion”.
  - Injection by melanocyte of melanin granules into a keratinocyte (exocytosis from melanocyte coupled with endocytosis to keratinocyte).

- Because of rapid transfer more melanin found in keratinocyte than melanocyte.

- Melanin accumulate on sunny side of nucleus
  - protection of nucleus from UV

- Dark skin absorbs and disperse UV better than light skin

* melanocyte production is fixed but production of melanin isn’t fixed but depend on two thing (which make racial differences):

1) Degree of melanin dispersion. (distribution)

2) Lysosomal action on melanosomes (degradation)
   - Light races - melanin rapidly broken down
   - Dark races - melanin granules more resistant within st. spinosum
   - Tanning increase melanin concentration not number of melanosomes.
Other causes of skin color

- Carotene in dermis
  - Yellow-orange pigment *(precursor of vitamin A)*
  - Found in stratum corneum & dermis
- Hemoglobin
  - Red, oxygen-carrying pigment in blood cells
  - If other pigments are not present, epidermis is translucent so pinkness will be evident

Langerhans cells (WBC from bone marrow)

- Appearance
  - Clear cells, generally has a dendritic appearance
- Location
  - St. basale and spinosum,
  - Process extend toward surface
- Act as antigen presenting cells with some phagocytic activity
- Absence of tonofibrils and desmosomes
- May contain melanin granules due to phagocytic activity of damaged keratinocytes
- Responsible for the initial allergic reaction due to contact hypersensitivity
- Bone marrow originated cell