TEXTBOOK

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DERMATOVENEROLOGY

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CONTENTS

Chapter 1

AN OVERVIEW OF SKIN AND ITS APPENDAGES. MORPHOLOGICAL ELEMENTS OF SKIN RASH

This is the most important chapter of this textbook. Why?

Because if the information in this chapter is well understood and mastered, all tasks are completed, it will be understood that, the whole foundation of this discipline is found in this chapter, especially the basis and fundamental knowledge of skin pathologies.

Firstly, you will be introduced to (or reminded of) the structure of the skin and its appendages. This will help you get a good idea of the ethiologyethiology and pathogenesis of dermatoses, and then proceed to the study of a completely new and very interesting subsection about the morphological elements of skin rashes.

In your training, you are now perhaps familiar with or might have heard in other medical disciplines the expressions for practicing doctors: “spot diagnosis” or “diagnosis at first sight”.

In dermatovenerology, this is only possible with a good knowledge of the morphological elements of the skin rash, i.e. it will help you in the future to recognize certain diseases in one clinical picture or conduct a differential diagnosis between them. In other words, for dermatovenerologist the ability to perform careful visual analysis is of utmost importance. Abu Ali Ibn Sina also said, “a Doctor must have the eye of a Falcon”.

However, before you start reading, kindly note the following important points:

- When reading this chapter and all subsequent chapters do not skip, rather, carefully study all the text, drawings, diagrams and figures.
- Try as much as possible to solve all the tasks and assignments at the end of each chapter.

- Do not proceed to the next chapter without ensuring that the previous chapter (materials) has been well assimilated. This can be ascertained if one can correctly answer all tasks and assignments (i.e. your answers coincide with answers provided in the book). **If you make a mistake, read this section again.**

If there is no desire to re-read, return to this page and reread this phrase of I.P. Pavlov (Nobel laureate in medicine and physiology): "Think, think: if you do not get used to thinking and making a living organism and the whole course of life the subject of persistent and passionate thinking, all your future activities will be reduced to just craft which will disappoint you and lead to despair".

1.1. THE STRUCTURE OF THE SKIN AND ITS APPENDAGES

The skin is multifunctional and is the largest organ of the human body. It covers/protects the body, serves as a boundary separating it from the external environment, and is closely interconnected with all other organs and systems. In this regard, and to a certain extent, the skins plays an important role in a variety of physiological and pathological processes.

The skin covers the entire surface of the body. In the areas of natural openings (mouth, nose, urethra, vagina and anus) the skin thins into a mucous membrane.

The total area of the skin of an adult is 1.5–1.8 m^2. In a child, however, this depends on the age. In general this is about 18% of the body weight of an adult and 20% of the body weight of a new-born.

In the process of ontogenesis, the skin develops from two embryonic leaves — **outer (ectoderm)** and **middle (mesoderm)** and consists of two types of closely related tissue — **epidermal** and **connective**.

There are three parts of the skin (fig. 1.1):

- epidermis (epidermis);
- derma (derma);
- subcutaneous fat (subcutis), or hypodermis (hypodermis).

1.1.1. Epidermis

The epidermis and its appendages (hair, nails, sweat and sebaceous glands) develop from ectoderm. In the 2nd week of embryogenesis melanocytes penetrate into the basal layer of the epidermis from the neural crest.

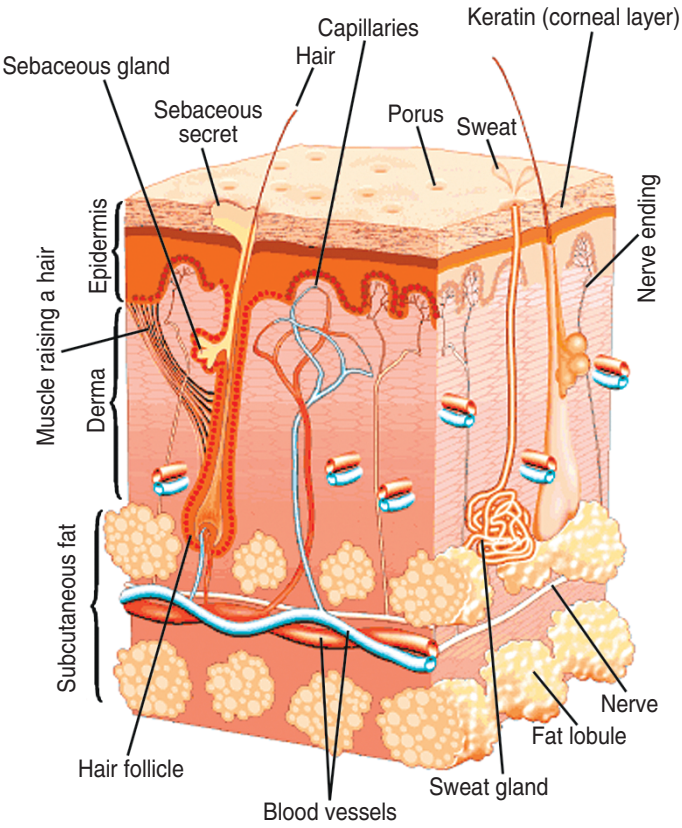

Fig. 1.1. The structure of the skin and appendages

In the epidermis there are three mandatory types of cells.

- Keratinocytes (epidermocytes) are presented in various evolutionary forms and make up the main cellular mass of the epidermis.
- Pigment cells (melanocytes).
- Immune cells (intra-epidermal macrophages).

In the epidermis, there are also Merkel cells, but they are neuro-receptor structures and are associated with nerve endings penetrating from the dermis.

The epidermis is a multi-layered flat keratinous epithelium, the thickness of which is 0.04 mm in the most tender places (eyelids), however, on rough surfaces (palms, soles) it may be up to 1.6 mm.

Layer of epidermis

In the epidermis there are five layers (fig. 1.2):

- *stratum corneum*;
- *stratum lucidum*;
- *stratum granulosum*;
- *stratum spinosum*;
- *stratum basale*.

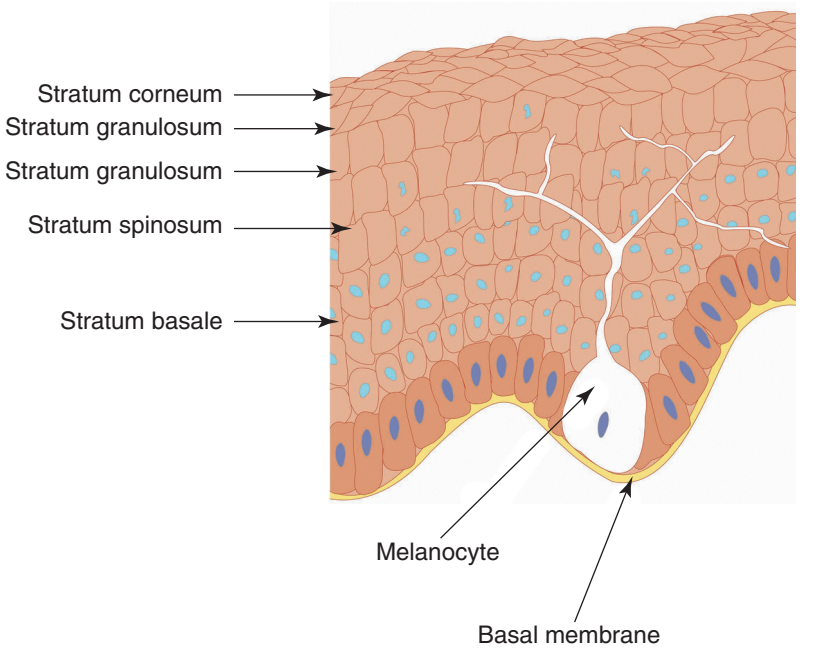

Fig. 1.2. Structure of the epidermis

The basal layer (*stratum basale*)

The basal layer consists of a series of cylindrical cells (basal keratinocytes), having mitotic activity. Among themselves, the keratinocytes of the basal layer are connected by desmosomes, and semi-desmosomes are attached to the basal membrane.

Semi-desmosomes are microscopic cytoplasmic cell outgrowths penetrating into the basal membrane and causing a strong connection of the epidermis with the basal membrane and the dermis.

There are two subpopulations of keratinocytes: one constantly proliferates, the second subpopulation is dormant (reserve). The main function of basal keratinocytes is a constant proliferation and regeneration of epidermal defects.

Melanocytes — are large spinous and pigment cells which lie on the basal membrane and form the basal layer of the epidermis. Melanocytes are in the mucous membrane, except the thick epidermis of the palms and soles, where these cells are absent. In adult humans, the number of melanocytes is approximately 10% of all epidermal cells (in new-borns — 3.7%, and in children — 7%). The number of melanocytic cells does not depend on race or gender. Melanocytes synthesize **melanin** pigment that protects the skin from the harmful effects of UV rays. Melanocytes produce melanin from tyrosine with the participation of the enzyme tyrosinase.

Spinous layer (*stratum spinatum*)

Located above the basal layer, the spinous layer consists of 3–8 rows of cells with "spikes". Spiked keratinocytes consist of a large number of outgrowths (desmosomes), penetrating into the recesses of neighbouring cells and connecting them like a "lightning" and forming so called **Bizzozero nodules**. All this gives the epidermis its strength and elasticity.

Langerhans cells (intraepidermal macrophages) are also located in the spinous layer and are cells with long processes reaching the basal membrane and granular layer. In the presence of inflammation, they can migrate to the dermis and lymph nodes. The feature that distinguishes Langerhans cells from other macrophages is the presence of special rod-shaped "tennis-racket" cytoplasmic **Birbeck granules** which contain the Kalone — the substance suppressing the proliferation of keratinocytes. Langerhans cells make up 2–7% of all epidermal cells, have mesodermal origin.

Basic functions of Langerhans cells:

- regulation of keratinocyte population;
- antigen presentation on t-helpers of lymphocytes, secretion of interleukins-1, -4, interferon, tumor necrosis factor (TNF), etc.;
- participation in immunopathological processes of the skin.

Granstein cells resemble Langerhans cells but lack Birbeck granules. They number 1–3% of all epidermal cells in total. Their functions include that of antigen-presenting cells for T-suppressors of lymphocytes.

The basal and spinous layers are collectively called **Malpighian layer**, or **germ layer** of the epidermis.

Granular layer (*stratum granulosum*)

It consists of 1–2 rows of cells (2–4 rows on the palms and soles) in the form of an elongated rhombus — granular keratinocytes. The characteristic feature

of the cells of this series is the presence of multiple cytoplasmic keratohyalin granules as well as Orlando granules, a lamellar body with lipid vesicles — keratinose. Later, these substances form a bilipid layer between the sharp pointed scales. The highly specialized epidermal lipids include ceramides, cholesterol, fatty acids, phospholipids and other lipid compounds.

Shiny layer (*stratum lucidum*)

The lucid layer looks like a shiny narrow structureless strip that separates the granular layer from the horny (available on the palms and soles).

Horny layer (*stratum corneum*)

The stratum corneum is the final product of the evolution of keratinocytes, consisting of a plurality of tile-like scales (corneocytes), which are necrotic and keratin-filled remains of keratinocytes. Corneocytes are tightly adjacent to each other, but on the surface, are in contact with the external environment are loosely packed and easily separated — physiological peeling, a process which is invisible to the naked eye. The thickness of the stratum corneum considerably varies on different parts of the skin (the largest — on the soles and palms, in the area of callus).

The corneocytes and the lipid layers of keratinases of the granular layer form a multilayered lipid structure in the stratum corneum and form the **epidermal lipid barrier** that protects the skin from transepidermal water loss and providing a water resistant epidermis. Epidermal lipid barrier also plays the role of a special intercellular cementing substance, providing the strength of adhesion of the structures of the stratum corneum and preserving the integrity of the skin. Epidermal ceramides not only retain water in the skin, but also regulate the rate of desquamation, affecting the differentiation of keratinocytes, and have a pronounced antimicrobial effect.

The cycle of progression of epithelial cells from the cells of the basal layer to the rejected Horny plates is normally 28 days.

The epidermis is separated from the dermis by a **basal membrane**, which is a specialized intercellular matrix. On electron microscopy, the basal membrane emits light and dense plates, as well as a plasmolemma. There are numerous pinocyte 'bubbles'. This indicates that the basal membrane actively participates in the metabolic processes between the epidermis and the dermis. Due to the absence of blood vessels in the epidermis, the epidermis is nourished by diffusion of nutrients through the basal membrane from the dermis.

Features of the epidermis structure in children

- *In children, the epidermis is thin, consists mainly basal, spiny and Horny layers.* The stratum corneum in children is not only thin, butis also loose.

All rows of cells contain nuclei. The processes of exfoliation of the stratum corneum in young children occur 4–5 times faster than in adults. Due to the absence of a granular layer in the epidermis of the infant skin, ceramides are practically not synthesized and there is a failure of the epidermal lipid barrier. These special structural features lead to the fact that the child's skin is easily vulnerable at the slightest adverse effects (hygiene, frequent bathing and use of soap, tight swaddling) and is prone to maceration.

- *The process of mitotic division is more intense in a child's skin than adults.* Mitosis not only occurs in the cells of the basal layer, but also appears partially in the spinous layer, which contributes to faster reparative processes (epithelialization) in cases of damage to the epidermis.
- *The weak connection of keratinocytes of the basal layer with each other*, as well as with the basal membrane associated with a small amount of desmosis and semi-desmosis in these cells is a very important feature of the child's skin. Due to this, the skin of children undergoes epidermolytic processes more offen than the adult skin. This leads to a violation of the dermal-epidermal connection and is clinically manifested by bullous dermatoses (pemphigus of new-borns, exfoliative Ritter dermatitis, bullous impetigo, etc.).
- There are fewer melanocytes in the child skin in comparison to the skin of adults, as well as up to 6 months age melocytes are functionally inactive and contain a small number of melanin granules, which determines the sensitivity of children's skin to ultraviolet radiation.
- The pH of skin of new-borns is slightly different than the skin of adult. The skin of the new-borns is almost neutral compared with a slightly acidic nature of the adult skin. However, it is slightly alkaline in seborrheic zones and folds due to the caseous lubrication in those areas. After 2–4 weeks of the child's life, the skin begins to shift into an acidic environment. This feature causes more frequent progression of pyoderma and candida infection in young children.

Task 2. Briefly pause reading and try to remember from histology, which cells are shown in fig. 1.3. In what layer of the epidermis are they located? What is their function? (Answers on p. 82.)

Task 3. Close the book for a while and remember what is the different name of a germinal layer of the epidermis. What layers does it consist of? Take the time to look for the answer in the end of the chapter, first think about it yourself. (Answers on p. 82.)

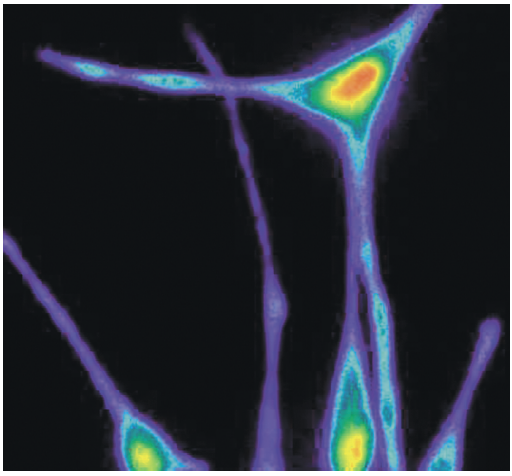

Fig. 1.3. For task 2

1.1.2. Dermis

The dermis consists of two layers: **papillary** and **mesh**.

The papillary layer is formed by loose connective tissue and capillary network, and the mesh layer is formed by dense fibrous unformed connective tissue. Both layers consist of three components:

- cells';
- base material;
- fibers'.

The dermis contains blood, lymphatic vessels and nerve endings.

The cells of the dermis:

- **Fibroblasts** are the main cells of the dermis. They provide synthesis of collagen, elastic and reticulin fibers, as well as of the main substance.
- **Mast cells** (mastocytes, tissue basophils) are precursors of blood stem cells and tissue analogues of basophilic blood leukocytes. The cytoplasm of mast cells contain specific granules with biologically active substances-histamine, heparin, serotonin and hyaluronic acid. These substances have a regulating effect on the vascular permeability of the skin and differentiation of various cells. They also participate in the progression of inflammatory and immune reactions and possess high migration ability.
- **Histiocytes** (tissue macrophages) carry out phagocytosis. Their cytoplasm has lysosomes containing hydrolytic lysosomal enzymes (colla-

genase, elastase, lysozyme, etc.), under whose effect the destruction of phagocytic particles takes place. Histiocytes secrete mediators-interleukin-1, α-interferon and TNF which activate and suppress the function and division of connective tissue cells and immunocompetent cells.

- **T-lymphocytes** — blood cells located around the blood and lymph vessels. If necessary, they are capable of quickly migrating to the lower parts of the epidermis through dermal tissue. There are three types of T-lymphocytes — **T-helpers**, **T-suppressors**, **T-killers**:
  - T-helpers activate the production of b-lymphocyte antibodies;
  - T-suppressors inhibit the inclusion of b-lymphocytes in differentiation and delay the production of antibodies;
  - T-killers-lymphocytes, independently carrying out the lysis of foreign cells.
- **Plasma cells (plasmocytes)** under normal conditions are rare to find in the dermis. They are usually found only around the vessels. *The function of plasma cells is the secretion of antibodies (IgA, IgM, IgG, etc.).*

Task 4. Look carefully at the fig. 1.4. Can you tell which of the above skin cells is depicted in the center? What other skin cells does it look like? How different is it from them? (Answers on p. 82.)

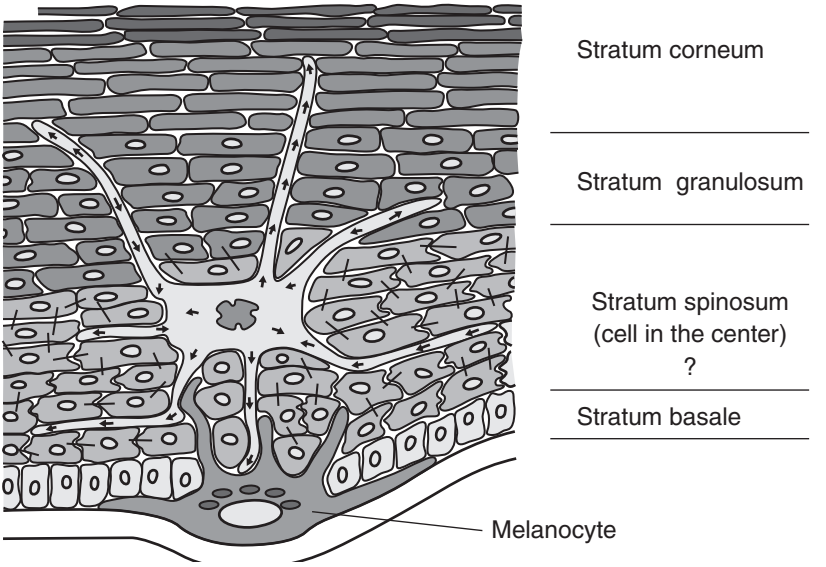

Fig. 1.4. For task 4

Fibers of the dermis

- ***Collagen fibers*** — the main fibers of the dermis are built from the same type of protein — collagen, which provides mechanical strength of the dermis.
- ***Elastic fibers*** form a vast thin network in the dermis and contain the protein called elastin which has elastic and contraction properties.
- ***Reticular fibers*** are located directly under the epidermis, which has a pronounced elastic properties. A lot of them are located especially around skin appendages (hair follicles, sweat glands), where they act as a support.

Connective tissue fibers of the dermis are located in a strictly defined direction, they are linear and form **Langer lines** (fig. 1.5). The skin is stretched more strongly in the direction perpendicular to the course of the fibers, and, therefore, the least noticeable cicatrix after the cut of the skin is formed when there is a wound along the fibers, which must be taken into account during surgery.

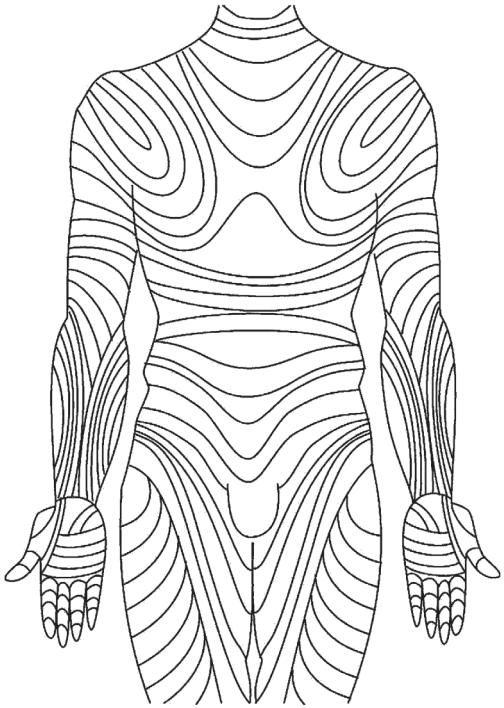

Fig. 1.5. Langer lines

The **main (amorphous) substance** is a gel which contains glycosaminoglycans, proteoglycans, hyaluronic acid, glycoproteins, fats, inorganic substances. They contribute to the absorption and retention of water in the tissues, providing cellular reactions, biochemical processes, and build up strength of the main substance of the connective tissue.

Vessels of the dermis

The boundary of the papillary and mesh layers is considered to be a branch of the superficial network of blood vessels, forming a horizontally positioned network: superficial and deep. The arteries are parallel to the veins.

The superficial plexus is represented by small vessels (capillaries, arterioles, venules) located in the papillary layer of the dermis. Capillaries depart vertically into the papillae, where they form the thinnest vascular branches in the form of loops and are responsible for microcirculation in the skin.

The deep vascular network is located on the border of the dermis with subcutaneous fat. The deep plexus consists of larger vessels in the retinal layer of the dermis and subcutaneous fat. Between the superficial and deep plexuses there are anastomoses.

There is a topographical and functional link between the blood vessels and lymphatics, forming the superficial and deep networks.

The structure of the dermis in children

The dermis as well as other structures in new-borns and infants is much thinner than in adults. The border between the epidermis and the dermis is smooth and has a small dermal papillae (except for the skin of the palms and soles). The dermis is dominated by low-differentiated connective tissue cells and thin collagen fibers.

Among the cellular elements common to the skin: histiocytes, reticulocytes, fibrocytes, plasmocytes, lymphocytes — a lot of mast cells (mastocytes), release biologically active substances and enzymes (histamine, heparin, hyaluronidase, etc.). These substances and enzymes prepare the child's skin physiologically to fight off common allergic and inflammatory reactions. The spaces between the cells and fibers are filled with connective tissue substances, one most important example is mucopolysaccharides (hyaluronic acid and chondroitin sulphate), which has high moisture-retaining properties. These polysaccharides in the skin of children make the infant skin more moisturous than adult skin. Water provides good turgor of children's skin, as well as contributes to a more rapid spread of inflammatory, allergic and intoxication processes.

The blood vessels of the skin in children also have certain characteristics.