

Exploring the Embryological Origin, Anatomy, and Histological Structure of the Skin

Florica Voiță-Mekereș^{1,2*}

¹Department of Morphological Disciplines, Faculty of Medicine and Pharmacy, University of Oradea, 410087 Oradea, Romania.

²Bihor Clinical Emergency County Hospital, Oradea, Romania.

*E-mail ✉ res_florina@yahoo.com

Received: 10 March 2023; Revised: 27 June 2023; Accepted: 27 June 2023

ABSTRACT

The skin acts as the interface between the body and its external environment and represents the interconnectedness of all the organs and systems in the human organism. Its structure and positioning play a central role in the overall functioning of the body and, at the same time, contribute to the aesthetic appearance. This study aims to investigate the embryonic origins of the skin, its anatomical composition, and histological structure. The skin consists of two main components: the epidermis, which arises from the ectoderm, and the dermis, which develops from the mesoderm. The key functions of the skin include safeguarding the body, regulating temperature, controlling fluid loss, supporting immunity, and facilitating sensory perception. The blood supply to the skin originates from arterial branches or as terminal branches of the muscular vessels. Specialized sensory structures are embedded within the skin that allow it to respond to various stimuli, such as free nerve endings, Merkel cells, Meissner's corpuscles, Pacinian corpuscles, Krause bulbs, Ruffini corpuscles, and proprioceptors for temperature regulation. Skin injuries can lead to significant emotional and social repercussions, such as feelings of alienation, estrangement from loved ones, possible job loss, neurotic disorders, and other negative social outcomes.

Keywords: Skin, Skin anatomy, Embryological origin, Histological structure

How to Cite This Article: Voiță-Mekereș F. Exploring the Embryological Origin, Anatomy, and Histological Structure of the Skin. *Interdiscip Res Med Sci Spec.* 2023;3(2):10-6. <https://doi.org/10.51847/3SqO2bNKNC>

Introduction

Since ancient times, an individual's physical appearance has significantly influenced their social standing, role, and interactions with others. It has been a critical factor in determining one's position within societal hierarchies, influencing upward or downward movement on the social scale. In modern times, an appealing appearance plays a vital role in achieving success across various social contexts, with women typically being the primary focus, although as gender equality progresses, men's physical appearance is increasingly valued [1-3].

In certain high-paying fields with minimal complexity, such as advertising, modeling, social media, and television, appearance is often the deciding factor for participation. This emphasizes the importance of skin characteristics in defining beauty standards. Scars affecting areas crucial to non-verbal communication or altering facial symmetry can result in significant aesthetic damage, which is primarily felt in both personal and professional contexts. Additionally, any unsightly marks or scars cause distress for the individual affected [4-6].

The goal of this research is to examine the embryological origin, anatomical features, and histological composition of the skin.

Results and Discussion

Skin: definition and embryological origins

The skin covers the entire external surface of the body, serving as the first line of defense against external elements such as toxins, bacteria, viruses, ultraviolet radiation, and extreme temperatures. Moreover, the skin plays several

other vital roles, including thermoregulation via sweating, fluid retention, immune function, and sensory perception. As the largest organ in the body, the integument makes up roughly 16% of a person's total weight, with an average surface area of 1.2 to 2.3 m² in adults [7, 8].

The skin is composed of three main layers: the epidermis, which originates from the ectoderm; the dermis, which comes from the mesoderm; and the subcutaneous tissue or hypodermis, which has a distinct structure. The hypodermis consists of loose connective tissue and a fatty layer known for its fat cells, forming the macroscopic counterpart of the superficial fascia, which allows the skin to be loosely attached to underlying structures [9].

The epidermis originates from the ectoderm, the same tissue that gives rise to the central nervous system. It is composed primarily of a keratinized, stratified squamous epithelium, along with less common cell types like Merkel cells, melanocytes, and Langerhans cells. Melanocytes are responsible for pigmentation and originate from neural crest cells, while Langerhans cells, which play a role in antigen processing, are derived from the bone marrow. Merkel cells, which detect pressure, also come from neural crests [10, 11].

There are two main types of skin: thick, hairless, or glabrous skin, and thin, hairy skin [12].

The epidermis itself is divided into 5 layers of keratin-producing cells: the basal (germinal) layer, the spinous layer, the stratum granulosum, the stratum lucidum, and the stratum corneum.

The basal layer consists of a single row of basophilic cells, either cylindrical or cuboid in shape, located at the dermo-epidermal junction, directly attached to the basal membrane of the epithelium. Desmosomes link the cells, while hemidesmosomes anchor them to the basal membrane. This layer contains stem cells with high mitotic activity, enabling continuous renewal of the spinous layer. Epidermal cell turnover occurs every fifteen to thirty days, depending on age and the area of the body [13, 14].

The spinous layer comprises cuboidal cells with centrally positioned nuclei and fine extensions in the cytoplasm that house bundles of keratin fibers, termed tonofilaments. At the top of this layer, desmosomes are visible, contributing to the intercellular adhesion and enhancing the skin's resistance to mechanical wear. These structures, akin to those found in plants, help ensure cohesion. The Malpighian layer, located here, is where stem cells reside, playing a key role in replenishing the skin's cells [15].

The granular layer, located next, consists of 3 to 5 rows of polygonal cells that are flattened and contain keratohyalin granules. These cells lack distinct membranes. This layer forms a vital barrier, preventing the ingress of foreign materials and playing an important role in the skin's overall impermeability. Above it lies the translucent stratum lucidum, composed of flattened cells that stain eosinophilic. The outermost stratum corneum consists of 15-20 layers of flattened, non-nucleated cells filled with keratin. These cells are shed continuously as part of the skin's renewal process [16, 17].

The dermis, the second major layer of the skin, is primarily mesodermal in origin. It is made up of fibroblasts, collagen, elastic fibers, and blood vessels. The differentiation of the dermis begins in the fourth week of embryonic development, during which ectodermal and mesodermal tissues proliferate. This period also sees the formation of specialized structures like hair, nails, sweat glands, and teeth [18].

Research indicates that both the epidermis and dermis contribute to the development of hair follicles and teeth, whereas nails are solely formed by the epidermis. At birth, the skin has already reached its multilayered form, undergoing continuous renewal throughout life as older layers are replaced. The thickness of the skin varies depending on factors like age, gender, and the specific body region. The dermis is the primary determinant of skin thickness, with the epidermis generally remaining consistent. Skin thickness is at its greatest on the palms and soles, about 1.5 mm, and thinnest around the eyelids, at approximately 0.05 mm [19].

Skin structure

The epidermis, as the outermost skin layer, is exposed to the environment and is avascular, relying entirely on the dermis beneath it for nutrients via diffusion. It is composed of keratinocytes at different stages of differentiation, from the least differentiated in the deepest layers to the most mature near the surface. The epidermis consists of four primary layers: the basal or germinal layer, the spinous layer, the granular layer, and the corneal layer.

Keratinocytes

The basal layer sits directly above the dermo-epidermal junction and is composed of a single layer of keratinocytes attached to the basement membrane by hemidesmosomes. As these keratinocytes mature, they migrate towards the surface, becoming more differentiated as they ascend. By the time they reach the stratum corneum, these cells are fully differentiated and shed as part of the skin's continual renewal process [20].

Melanocytes

Melanocytes are specialized cells that generate melanin, a pigment that absorbs ultraviolet (UV) radiation from sunlight, helping to mitigate its harmful mutagenic effects. The melanin is stored in melanosomes, which are transferred to adjacent keratinocytes through dendritic processes. These melanosomes are transferred to keratinocytes by phagocytosis and stored as pigment granules. Melanocytes reside in the basal layer of the epidermis and are also found in the retina, hair follicles, and leptomeninges. In sun-exposed areas, the melanocyte to keratinocyte ratio is approximately 1:4, whereas it is 1:30 in less exposed regions. Interestingly, the number of melanosomes remains the same across both genders and races [21, 22].

Differences in pigmentation between individuals arise from variations in the size of melanosomes. Sun exposure triggers the release of hormones such as melanocyte-stimulating hormone (MSH), cortico-stimulating hormone, estrogen, and progesterone, which together activate melanin production. While melanin is created in melanocytes, it is stored in the surrounding epithelial cells, which hold greater quantities of melanin than the melanocytes themselves [23]. The primary factors influencing skin pigmentation are:

- The rate at which melanocytes produce melanin.
- The transfer of melanin to keratinocytes.
- The storage of melanin granules within keratinocytes.

Melanocytes secrete two pigments: eumelanin, which produces a dark brown hue, and pheomelanin, known for its high cysteine content and specific to red hair. As people age, the number of melanocytes diminishes because these cells are unable to regenerate [24].

Langerhans cells

Langerhans cells, derived from the bone marrow, are primarily located within the basal, spinous, and granular layers of the epidermis. These specialized cells act as antigen-presenting cells, playing an essential role in immune responses. They can ingest foreign substances, break them into smaller peptide fragments, which then bind to the major histocompatibility complex. These fragments are subsequently presented to lymphocytes, initiating an immune reaction [25].

Merkel cells

Merkel cells, which arise from the neural crest, are found in areas like the palms, genital region, nail beds, and other skin regions. They are mainly responsible for the sensation of fine touch and are believed to function as mechanoreceptors. However, some research suggests that these cells may be part of the diffuse neuroendocrine system. The dermis comprises two layers: the superficial papillary dermis and the deeper reticular dermis. The papillary dermis is thin and consists of loose connective tissue rich in elastic fibers, reticular fibers, collagen, and capillaries. The reticular dermis, which is thicker, is made up of dense connective tissue containing larger blood vessels, as well as elastic and collagen fibers arranged in parallel layers. This layer also contains lymphatic vessels, fibroblasts, mast cells, nerve endings, and epidermal appendages. These components are embedded in a gelatinous matrix that includes mucopolysaccharides, glycoproteins, and chondroitin sulfate [10].

The deeper dermal region is uneven, with the adipose layer at the subcutaneous level acting as a cushioning structure for the skin.

Fibroblasts make up most of the cells in the dermis and are responsible for producing procollagen and elastic fibers. Procollagen is processed by enzymes to form collagen, which then arranges into a strong, reticulated network. This collagen framework is essential for providing the dermis with the durability and strength necessary to resist mechanical stresses. Collagen represents about 70% of the dermal weight, with 85% of it being type I collagen and 15% type III collagen. Although elastic fibers account for less than 1% of the dermis' weight, they play a critical role in enabling the skin to return to its original shape after being stretched [26].

Dermo-epidermal junction

The dermo-epidermal junction, a wavy basement membrane, ensures the connection between the epidermis and dermis layers. This structure includes two distinct laminae: the lamina lucida, which is thin and situated against the basal layer of keratinocytes, and the lamina densa, a thicker layer in direct contact with the dermis. The dermal papillae, which contain capillaries and lymphatic vessels, extend perpendicularly toward the epidermis. These finger-like projections align with similar formations in the epidermis, enhancing the interface area for the

exchange of essential nutrients, oxygen, and metabolic by-products between the dermis and the avascular epidermis [27].

Accessory glands of the epidermis

Epidermal appendages are intradermal structures, lined by epithelial cells, which play a critical role in the regeneration of skin. These appendages, which include sebaceous glands, sweat glands, apocrine glands, mammary glands, and hair follicles, are typically located within the deeper layers of the dermis and may extend into the hypodermis. Their unique capacity for regeneration is especially valuable in situations where the epidermis is damaged, such as in burns or abrasions. Sebaceous glands, or holocrine glands, are found across the body, excluding areas like the palms, soles, and the back of the feet. They are particularly abundant on the scalp and face, where they are frequently linked to acne formation. These glands secrete sebum, an oily mixture containing triglycerides, ceruminous esters, cholesterol esters, squalene, and cholesterol, which lubricates the skin and provides protection against moisture loss and physical damage.

Eccrine sweat glands are distributed across almost the entire body, except for specific areas such as the lips, external auditory canal, and genital regions. The highest concentrations are found on the palms, soles, and armpits. Each gland consists of a coiled secretory portion deep in the dermis that leads to the epidermis via a straight duct. Their main role is to produce sweat, which helps regulate body temperature by evaporative cooling [28, 29].

The hypothalamus governs the activity of sweat glands, activating them through sympathetic nervous control when the body temperature rises above normal levels [30].

Apocrine and mammary glands

Apocrine glands, although structurally similar to eccrine glands, are functionally distinct. These glands are primarily located in the axillary (armpit) area, the genital region, and in modified forms like ceruminous glands in the ears and Moll's glands in the eyelids. They also include the mammary glands. Apocrine glands only become active after puberty, suggesting that they may have a vestigial function. The mammary glands are essentially specialized versions of the apocrine glands [31].

Hair follicles

Hair follicles are structures that involve both the epidermis and dermis layers. These follicles are distributed across nearly the entire body, with exceptions such as the palms, soles, clitoral region, labia minora, glans penis, as well as portions of fingers, toes, and mucocutaneous junctions. The sebaceous glands, often located near hair follicles, are not found on the skin's surface directly but rather as part of the pilosebaceous unit. The base of the hair follicle, known as the hair bulb, is located deep within the dermis. In the facial region, the hair follicle may extend into the subcutaneous fat, enhancing the skin's ability to heal from deeper wounds. Hair growth follows two distinct phases: the active growing phase (anagen) and a resting phase (telogen), with a transitional phase (catagen) in between. The length of the anagen phase is directly linked to the length of the hair. This phase varies depending on the location on the body [32].

Subcutaneous tissue

The hypodermis, or subcutaneous tissue, consists of connective tissue that helps anchor the skin to the underlying structures. It contains adipocytes, which vary in size according to the person's nutritional status.

Skin phototype

The color of the skin is primarily influenced by the amount of melanin pigment present, which can be inherited or influenced by various environmental and physiological factors. Hormonal changes, like those during pregnancy, can alter the production and distribution of melanin. Additional factors influencing skin pigmentation include the levels of carotene and melanin, the density of blood vessels in the dermis, and the oxygenation level of blood flowing through them [33].

The Fitzpatrick scale classifies the skin's response to ultraviolet radiation based on individual tanning and sunburn history. This scale, which ranges from I to VI, is useful for assessing skin pigmentation before treatments like skin resurfacing. Type I skin is extremely fair, often freckled, burns easily upon UV exposure, and does not tan [34-36].

Vascularization of the skin

The skin receives its vascular supply from vessels that branch off from deeper structures. These vessels create a network that spans from the bone through to the skin, forming what is referred to as an angiotome. Adjacent vascular regions, known as angiosomes, are linked by vessels of varying sizes, ranging from small to medium caliber. Cutaneous blood vessels either stem directly from arteries, such as perforating septo-cutaneous or fasciculo-cutaneous vessels, or from the terminal branches of muscular vessels, referred to as perforating musculo-cutaneous vessels. As these vessels make their way towards the skin, they pass through connective tissue networks and give off branches to nearby tissues such as muscle, fascia, nerves, bone, and adipose tissue. The vessels that emerge from the deep fascia travel through intermuscular and intramuscular septa near tendons, ultimately reaching the skin and forming the dermal and subdermal vascular networks [35].

The dermis houses two major vascular plexuses—superficial and deep—that run horizontally. These networks are interconnected by perpendicular vessels. Cutaneous vessels link to each other to form a continuous circulatory network throughout the skin. Parallel to the blood vessels are the lymphatic vessels, which play a key role in transporting plasma, proteins, pathogens, and antigenic particles. Lymphatic capillaries, found in the dermal papillae's interstitial spaces, are blind-ended and non-valvular. These capillaries drain into valvular plexuses in the dermis and subdermis, eventually merging to form larger lymphatic vessels that pass through lymph nodes before draining into the venous system, close to the junction of the subclavian and internal jugular veins [36].

Skin innervation

The ability to perceive sensory stimuli is essential for protecting the body from harmful forces, such as pressure, trauma, and extreme temperatures. Specialized sensory structures within the skin detect different types of stimuli. Merkel cells, located in the epidermis and along the ridges of the skin as well as around hair follicle sheaths, along with Meissner's corpuscles found in the dermal papillae, are responsible for sensing light touch. These receptors are concentrated in high density at the fingertips [37].

Pacinian corpuscles, found deeper in the dermis and hypodermis, are sensitive to pressure. According to Sherrington, tactile sensitivity is categorized into two types: protopathic, which is a vague, diffuse sense of touch, and epicritic, which refers to fine, precise touch. Pain is detected by free nerve endings in the basal layer of the epidermis, and it is perceived when the intensity of stimuli, such as temperature or touch, exceeds a certain threshold. Krause bulbs sense cold, while Ruffini corpuscles are responsible for detecting heat. Proprioceptors for both temperature extremes are located in the outer dermis. The nerves that innervate the skin follow the paths of the blood vessels.

A dermatome refers to the specific area of the skin innervated by a single spinal nerve. These dermatomes can overlap, which is important to consider when performing anesthesia, particularly during nerve blocks [38, 39].

Conclusion

The skin functions as a vital barrier between the human body and its external surroundings, acting as an integrative component that connects and supports the various organs and systems of the body. Its structural characteristics and external positioning grant it a fundamental role in maintaining physiological balance, while also contributing to personal appearance and identity. Damage or alterations to the skin — particularly following injury — may have profound psychological and social effects, potentially disrupting daily life, limiting social interactions, and in certain cases, leading to employment difficulties, emotional disturbances, or unfavorable societal reactions.

Acknowledgments: None

Conflict of Interest: None

Financial Support: None

Ethics Statement: None

References

1. Khavkin J, Ellis DA. Aging skin: histology, physiology, and pathology. *Facial Plast Surg Clin North Am.* 2011;19(2):229-34. doi:10.1016/j.fsc.2011.04.003deleted

2. Căiță GA, Maghiar T, Bodog FD, Maghiar L, Voiță-Mekereș F, Lascu CF. A review of social factors affecting women's tendency to cosmetic surgery. *Pharmacophore*. 2023;14(1):111-5. doi:10.51847/GOEDyJpSvD
3. Mekereș F, Voiță GF, Mekereș GM, Bodog FD. Psychosocial impact of scars in evaluation of aesthetic prejudice. *Rom J Leg Med*. 2017;25:435-8.
4. Mekeres GM, Voiță-Mekereș F, Tudoran C, Buhaș CL, Tudoran M, Racoviță M, et al. Predictors for estimating scars' internalization in victims with post-traumatic scars versus patients with postsurgical scars. *Healthcare (Basel)*. 2022;10(3):550. doi:10.3390/healthcare10030550
5. Voiță-Mekeres F, Buhaș CL, Mekeres GM, Tudoran C, Racovita M, Faur CI, et al. Mekeres' psychosocial internalization scale: a scale for the evaluation of aesthetic prejudice in victims of accidents and violence. *Healthcare (Basel)*. 2021;9(11):1440.
6. Pașcalău AV, Cheregi CD, Mureșan MȘ, Șandor MI, Huniadi CA, Nikin Z, et al. CD4+ CD25+ regulatory T-cells role in tumor microenvironment of the squamous cell carcinoma. *Rom J Morphol Embryol*. 2021;62(1):249-53.
7. Tienda-Vázquez MA, Hanel JM, Márquez-Arteaga EM, Salgado-Álvarez AP, Scheckhuber CQ, Alanis-Gómez JR, et al. Exosomes: a promising strategy for repair, regeneration and treatment of skin disorders. *Cells*. 2023;12(12):1625. doi:10.3390/cells12121625
8. Zouboulis CC, Makrantonaki E. Clinical and laboratory skin biomarkers of organ-specific diseases. *Mech Ageing Dev*. 2019;177:144-9. doi:10.1016/j.mad.2018.08.003
9. Visscher MO, Carr AN, Narendran V. Epidermal immunity and function: origin in neonatal skin. *Front Mol Biosci*. 2022;9:894496. doi:10.3389/fmolb.2022.894496
10. Lee J, Rabbani CC, Gao H, Steinhart MR, Woodruff BM, Pflum ZE, et al. Hair-bearing human skin generated entirely from pluripotent stem cells. *Nature*. 2020;582(7812):399-404. doi:10.1038/s41586-020-2352-3
11. Tudoran C, Tudoran M, Abu-Awwad A, Cut TG, Voiță-Mekereș F. Spontaneous hematomas and deep vein thrombosis during the recovery from a SARS-CoV-2 infection: case report and literature review. *Medicina (Kaunas)*. 2022;58(2):230. doi:10.3390/medicina58020230
12. Mekeres GM, Buhaș CL, Csep AN, Beișanu C, Andreescu G, Marian P, et al. The importance of psychometric and physical scales for the evaluation of the consequences of scars-a literature review. *Clin Pract*. 2023;13(2):372-83. doi:10.3390/clinpract13020034
13. Goleva E, Berdyshev E, Leung DY. Epithelial barrier repair and prevention of allergy. *J Clin Invest*. 2019;129(4):1463-74. doi:10.1172/JCI124608
14. Mekeres GM, Buhaș CL, Bulzan M, Marian P, Hozan CT. Objective criteria in evaluating the consequences of the posttraumatic scars. *Pharmacophore*. 2022;13(1):56-61.
15. Cavalu S, Simon V, Albon C, Hozan C. Bioactivity evaluation of new silver doped bone cement for prosthetic surgery. *J Optoelectron Adv Mater*. 2007;9(3):690.
16. Wertz P. Epidermal lamellar granules. *Skin Pharmacol Physiol*. 2018;31(5):262-8. doi:10.1159/000491757
17. Nicoara ND, Varga D, Voita-Mekeres F, Galea-Holhos L, Andreescu G, Costas L. Study of basic emotions in the general population using the Likert scale. *Pharmacophore*. 2023;14(4):14-21. doi:10.51847/tjyOah1VwM
18. Voiță-Mekereș F, Voiță GF, Pogan MD, Delcea C, Manole F, Mekereș GM, et al. Clinical considerations of dental longevity from the lateral area. *Pharmacophore*. 2023;14(3):100-6.
19. Alibardi L. General aspects on skin development in vertebrates with emphasis on sauropsids epidermis. *Dev Biol*. 2023;501:60-73. doi:10.1016/j.ydbio.2023.05.007
20. Suman S, Domingues A, Ratajczak J, Ratajczak MZ. Potential clinical applications of stem cells in regenerative medicine. *Adv Exp Med Biol*. 2019;1201:1-22. doi:10.1007/978-3-030-31206-01
21. Chen J, Li S, Li C. Mechanisms of melanocyte death in vitiligo. *Med Res Rev*. 2021;41(2):1138-66. doi:10.1002/med.21754
22. Davidescu L, Chanez P, Ursol G, Korzh O, Deshmukh V, Kuryk L, et al. Late breaking abstract – masitinib in severe asthma: results from a randomized, phase 3 trial. *Eur Respir J*. 2020;56(64):4612.
23. Agar N, Young AR. Melanogenesis: a photoprotective response to DNA damage? *Mutat Res*. 2005;571(1-2):121-32.
24. Laiho L, Murray JF. The multifaceted melanocortin receptors. *Endocrinology*. 2022;163(7):bqac083. doi:10.1210/endo/bqac083

25. Rajesh A, Wise L, Hibma M. The role of Langerhans cells in pathologies of the skin. *Immunol Cell Biol.* 2019;97(8):700-13. doi:10.1111/imcb.12253
26. Shigematsu T, Koiwa F, Isaka Y, Fukagawa M, Hagita K, Watanabe YS, et al. Efficacy and safety of upacicalcet in hemodialysis patients with secondary hyperparathyroidism: A randomized placebo-controlled trial. *Clin J Am Soc Nephrol.* 2023;18(10):1300-9. doi:10.2215/CJN.0000000000000253
27. El Genedy-Kalyoncu M, Richter C, Surber C, Blume-Peytavi U, Kottner J. The effect of a basic skin care product on the structural strength of the dermo-epidermal junction: an exploratory, randomised, controlled split-body trial. *Int Wound J.* 2022;19(2):426-35. doi:10.1111/iwj.13643
28. Lacouture ME, Patel AB, Rosenberg JE, O'Donnell PH. Management of dermatologic events associated with the nectin-4-directed antibody-drug conjugate enfortumab vedotin. *Oncologist.* 2022;27(3):e223-32. doi:10.1093/oncolo/oyac001
29. Mekereș GM, Buhaș CL, Tudoran C, Csep AN, Tudoran M, Manole F, et al. The practical utility of psychometric scales for the assessment of the impact of posttraumatic scars on mental health. *Front Public Health.* 2023;11:1103714. doi:10.3389/fpubh.2023.1103714
30. Tan CL, Knight ZA. Regulation of body temperature by the nervous system. *Neuron.* 2018;98(1):31-48. doi:10.1016/j.neuron.2018.02.022
31. Shah A, Tsianou Z, Suchak R, Mann J. Apocrine chromhidrosis. *Am J Dermatopathol.* 2020;42(10):e147-8. doi:10.1097/DAD.0000000000001712
32. Usmani AS. Hair follicle bulb region: a potential nidus for the formation of osteoma cutis. *Cutis.* 2021;107(1):E31-4. doi:10.12788/cutis.0180
33. Passeron T, Lim HW, Goh CL, Kang HY, Ly F, Morita A, et al. Photoprotection according to skin phototype and dermatoses: practical recommendations from an expert panel. *J Eur Acad Dermatol Venereol.* 2021;35(7):1460-9. doi:10.1111/jdv.17242
34. Shope CN, Andrews LA, Neimy H, Linkous CL, Khamdan F, Lee LW. Characterizing skin cancer in transplant recipients by fitzpatrick skin phototype. *Dermatol Ther (Heidelb).* 2023;13(1):147-54. doi:10.1007/s13555-022-00858-z
35. Coroi MC, Bakraoui A, Sala C, Țica O, Țica OA, Jurcă MC, et al. Choroidal melanoma, unfavorable prognostic factors. Case report and review of literature. *Roman J Morphol Embryol.* 2019;60(2):673-8.
36. Holhoș LB, Coroi MC, Lazăr L. Observations on refractive status and risk factors for visual impairment in children with disabilities. *Medicina.* 2021;57(5):403.
37. Lee HJ, Hong YJ, Kim M. Angiogenesis in chronic inflammatory skin disorders. *Int J Mol Sci.* 2021;22(21):12035. doi:10.3390/ijms222112035
38. Ogawa R. Keloid and hypertrophic scars are the result of chronic inflammation in the reticular dermis. *Int J Mol Sci.* 2017;18(3):606. doi:10.3390/ijms18030606
39. Laverdet B, Danigo A, Girard D, Magy L, Demiot C, Desmoulière A. Skin innervation: Important roles during normal and pathological cutaneous repair. *Histol Histopathol.* 2015;30(8):875-92. doi:10.14670/HH-11-610