

BASICS OF SKIN HISTOPOIOLOGY

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Annotation: The skin or cutis covers the entire outer surface of the body. Structurally, the skin consists of two layers which differ in function, histological appearance and their embryological origin. The outer layer or epidermis is formed by an epithelium and is of ectodermal origin. The underlying thicker layer, the dermis, consists of connective tissue and develops from the mesoderm. Beneath the two layers we find a subcutaneous layer of loose connective tissue or hypodermis, which binds the skin to underlying structures. Hair, nails and sweat and sebaceous glands are of epithelial origin and collectively called the appendages of the skin.

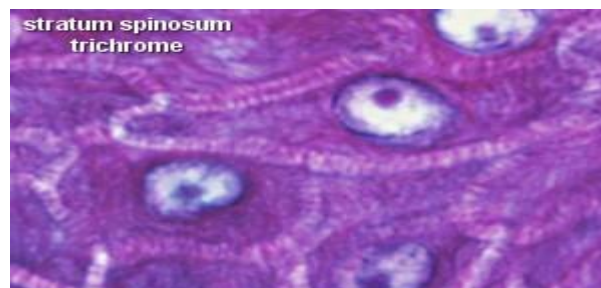
Key words: skin, layer, hypodermis, epithelium, epidermis .

The skin and its appendages together are called the integumentary system.

Skin, thick - H&E, trichromeA good starting point is to identify the main layers (epidermis, dermis and hypodermis) of the skin at low magnification. The three layers forming the skin can be identified in all skin sections. The epithelium forming the surface layer, the epidermis, is usually the darkest layer visible. Sublayers are visible in the epidermis. Their staining varies - not just between stains but also between different H&E stained preparations (possibly depending on tissue preservation and how fresh the staining solutions were). At the transition from the epidermis to the dermis, staining will become lighter. The lighter stained layer, the dermis, consists of dense irregular connective tissue. The dermis is much thicker than the epidermis. In thick skin, dermal papillae create a very irregular border between epidermis and dermis. The hypodermis is the lightest layer visible and consists mainly of adipose tissue. Dense connective tissue strands may extend from the dermis deep into the hypodermis and anchor the skin to underlying structures. The epidermis is a keratinised stratified squamous epithelium. The main function of the epidermis is to protect the body from harmful influences from the environment and against fluid loss. Five structurally different layers can be identified:

1. The stratum basale is the deepest layer of the epidermis (closest to the dermis). It consists of a single layer of columnar or cuboidal cells which rest on the basement membrane. Basal cells are the stem cells of the epidermis. Their mitotic activity replenishes the cells in more superficial layers as these are eventually shed from the epidermis. The renewal of the epidermis takes about 3 to 4 weeks in humans.

2. In the stratum spinosum, the cells become irregularly polygonal. The cells are often separated by narrow, translucent clefts. These clefts are spanned by spine-like cytoplasmic extensions of the cells (hence the name of the layer and of its cells: spinous cells), which interconnect the cells of this layer. Spines of cells meet end-to-end or side-to-side and are attached to each other by desmosomes. In addition to the usual organelles of cells, EM



shows membrane-bound lamellar granules in the cytoplasm of the spinous cells.

3. The stratum granulosum consists, in thick skin, of a few layers of flattened cells. Only one layer may be visible in thin skin. The cytoplasm of the cells contains numerous fine grains, keratohyalin granules. The keratohyalin is not located in membrane-bound organelles but forms "free" accumulations in the cytoplasm of the cells. The cells begin to release the contents of the lamellar granules. The lipids contained in the granules come to fill the entire interstitial space, which is important for the function of the epidermis as a barrier towards the external environment.

4. The stratum lucidum consists of several layers of flattened dead cells. Nuclei already begin to degenerate in the outer part of the stratum granulosum. In the stratum lucidum, faint nuclear outlines are visible in only a few of the cells. The stratum lucidum can usually not be identified in thin skin.

5. In the stratum corneum, cells are completely filled with keratin filaments (horny cells) which are embedded in a dense matrix of proteins. Individual cells are difficult to observe because (1) nuclei can no longer be identified, (2) the cells are very flat and (3) the space between the cells has been filled with lipids, which cement the cells together into a continuous membrane. In the EM, the cell membranes appear thickened and interdigitate with those of neighbouring cells. Closest to the surface of the epidermis, the stratum corneum has a somewhat looser appearance. Horny cells are constantly shed from this part of the stratum corneum.

The protection of the body by the epidermis is essentially due to the functional features of the stratum corneum.

Variations in the thickness of the epidermis (~0.1 mm in thin skin, 1 mm or more in thick skin) are mainly the result of variations in the thickness of the stratum corneum, although the other layers also vary in thickness. Cells of the epidermis of the skin will at some time of their life keratinise and are collectively also called keratinocytes.

Keratinisation should not be used as a synonym for the formation of the stratum corneum: other stratified squamous epithelia may become keratinised but may not form a stratum corneum in which cells join to form a horny cell membrane.

Suitable Slides

sections of skin - H&E, trichrome or van Gieson

Skin, thin - H&E and Skin, thick, trichrome The most superficial part of the epidermis is formed by the stratum corneum. Nuclei are not visible in this layer. Cell outlines may be visible at high magnification or, in the form of artefacts, as cracks or clefts in the stratum corneum. The stratum granulosum is formed by a single layer of very dark and flattened cells in thin skin. Several layers of cells containing keratohyalin granules are visible in thick skin. Polyhedral cells with clear outlines form the stratum spinosum. The stratum basale is formed by a single layer of cuboidal or columnar cells and delimits the epidermis from the dermis.

At high magnification, the basal cytoplasm of the basal cells seem to interdigitate with the underlying dermis. Similar to the dermal papilla, this irregular border at the cellular level, the dermal-epidermal junction, anchors individual basal cells firmly to the underlying dermis.

Identify and draw the epithelium in thick and thin skin. Identify in your drawing as many of the layers of the epidermis as possible.

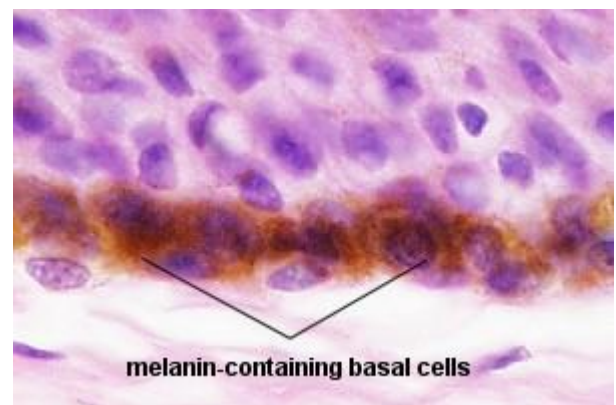
The red and yellow hues of the skin are due to haemoglobin in the red blood cells, which pass through the capillaries beneath the epidermis, and carotene, which accumulates in fat cells found in the dermis and hypodermis.

Melanocytes

The brown colour component is due to melanin, which is produced in the skin itself in cells called melanocytes (typically 1000-2000 / sq. mm). These cells are located in the epidermis and send fine processes between the other cells. In the melanocytes, the melanin is located in membrane-bound organelles called melanosomes. The cell bodies of melanocytes are difficult to distinguish in ordinary LM preparations, because the melanosomes are located mainly in the processes of the cells.

Melanocytes can transfer melanin to keratinocytes - mainly to the basal cells. The fine processes of melanocytes may invade keratinocytes and bud-off part of the melanocyte-cytoplasm, including the melanosomes, within the keratinocytes. Melanin protects the chromosomes of mitotically active basal cells against light-induced damage.

Pigmentation is not just under the control of light. Hormones produced by the pituitary and the adrenal glands also affect pigmentation. Diseases of these two endocrine organs often result in changes of pigmentation of the skin.



Although melanocytes are also ectodermal in origin, they are derived exclusively from the neural crest of the embryo, from where they migrate to all other parts of the body.

Langerhans Cells

are another cell type found within the epidermis. Morphologically they are not unlike melanocytes, but functionally they are more closely related to macrophages. They are important in immune reactions of the epidermis. Their fine processes form a network between the cells of the epidermis and phagocytose antigens which have entered the epidermis. Langerhans cells may only be temporary residents of the skin. If they have come into contact with an antigen, they can migrate to regional lymph nodes, where they initiate an immune response.

T-lymphocytes

are, like Langerhans cells, a group of cells functioning in the immune system. Some of them will be present in the epidermis. Together with Langerhans cells they are sometimes referred to as SALT, i.e. skin-associated lymphoid tissue.

The Dermis

The dermis is the thick layer of connective tissue to which the epidermis is attached. Its deepest part continues into the subcutaneous tissue without a sharply defined boundary. Its thickness is for this reason difficult to determine but 1-2 mm is a good guestimate for "average" skin. The dermis may be divided into two sublayers (again without a sharp boundary):

- The papillary layer consists of loose, comparatively cell-rich connective tissue, which fills the hollows at the deep surface (dermal papillae) of the epidermis. Capillaries are frequent. Collagen fibres appear finer than in the reticular layer.
- The reticular layer appears denser and contains fewer cells. Thick collagen fibres (5-10 μm) often aggregate into bundles (up to 100 μm thick). The fibres form an interlacing network, although their predominant direction is parallel to the surface of the skin. A preferred orientation of the collagen fibres is not visible in the sections, but the main orientation of the fibres differs in skin from different parts of the body. Usually, their main orientation will follow the "lines of greatest tension" in the skin (Kraissl lines). This is of some surgical importance since incisions parallel to these lines will heal faster and with less formation of scar tissue.

Kraissl lines have been defined in living humans. They not always coincide with the cleavage lines, which Langer defined (Langer's cleavage lines) about a century before Kraissl in cadavers.

Elastic fibres are found in both the papillary (fine fibres) and reticular (coarse fibres) layers. They can not be identified in H&E stained sections.

Suitable Slides

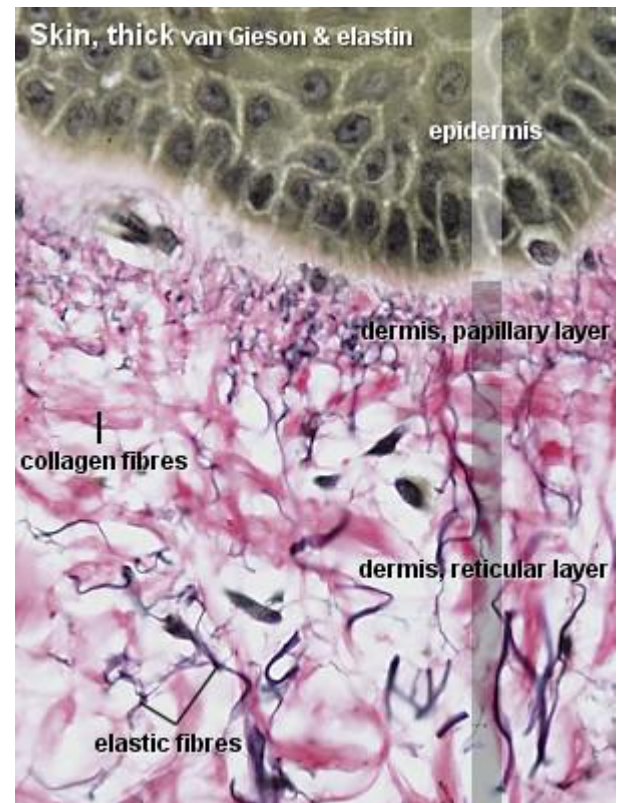
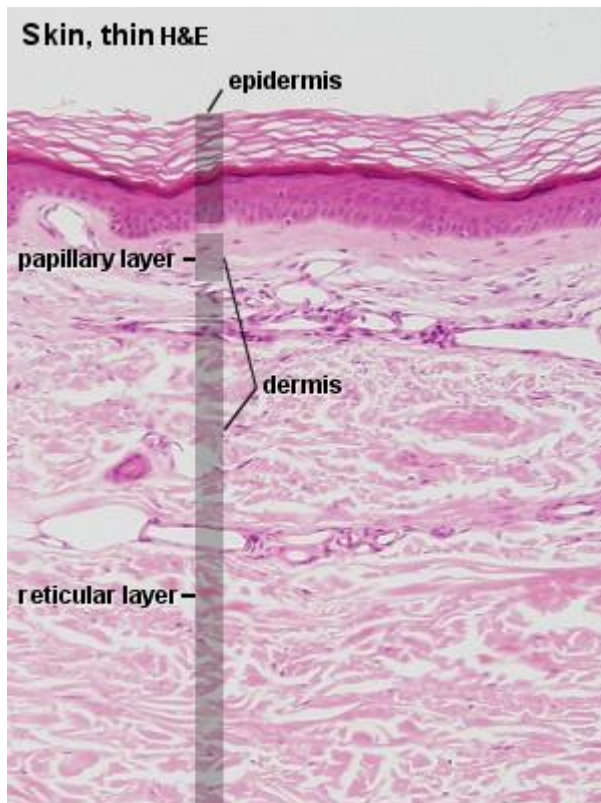
sections of skin - H&E, van Gieson

Van Gieson stained sections are particularly nice if the van Gieson stain has been combined with an elastin stain.

Skin, thin - H&E and Skin, thick - van Gieson & elastin

How easy it is to differentiate between the papillary and reticular layer of the dermis depends on the preparation - you may have to look at several preparations. Immediately beneath the epidermis you should see a layer which at low magnification appears rather evenly stained. At high magnification the stain should resolve into a fine network of collagen fibres, which blend with equally fine elastic fibres. Cells are more numerous in the papillary layer and you should see more nuclei in this area than in the deeper reticular layer. Also, the papillary layer contains the capillary network which supplies the epidermis, The reticular layer contains coarse collagen and elastic fibres and the larger vessels which feed into the capillary network of the papillary layer..

Draw part of the epidermis and the underlying dermis. Label the layers of the dermis and structures contained within them



Appendages of the Skin

Hair

A characteristic feature of the human skin is the apparent lack of hair (pili) on most of the body surface. This is actually not quite true. Most of the skin is haired although the hair in most areas is short, fine and only lightly pigmented. This type of hair is called vellus hair.

Truly hairless are only the palms of hands and soles of feet, the distal phalanges and sides of fingers and toes and parts of the external genitalia.

In those parts of the skin which we perceive as "hairy" we find terminal hairs. The free part of each hair is called the shaft. The root of each hair is anchored in a tubular invagination of the epidermis, the hair follicle, which extends down into the dermis and, usually, a short distance into the hypodermis. The deepest end of the hair follicle forms an enlargement, the bulb. Cells in the bulb are mitotically active. Their progeny differentiates into the cell types which form the hair and the cells that surround its root, the root sheath. Hair cells keratinise within the lower one-third of the hair follicle. Above this level it is not possible to identify individual cells within the hair. Each hair follicle has an associated bundle of smooth muscle, the arrector pili muscle. This muscle inserts with one end to the papillary layer of the dermis and with the other end to the dermal sheath of the hair follicle.

Hair growth is discontinuous. Hairs are lost and replaced by new ones. The hair follicle goes through different stages that reflect the discontinuous hair growth. Anagen is the phase of growth. The resting stage is called telogen. The length of the anagen is variable in different regions of the body - lasting only a few months for hair of the eyebrows and eyelashes but 2 to 5 years for hair of the scalp. Hair growth is controlled by a number of hormonal and hereditary factors and their interactions.

Suitable Slides

Sections of hairy skin or scalp - H&E

With a few exceptions (thick skin and skin covering parts of the external genitalia), all skin sections should contain a few hair follicles.

Skin, hairy - H&E

Hair follicles of terminal hair span the entire dermis and usually extend deep into the hypodermis. Most of them will be cut at odd angles and only a few good longitudinally or transversely cut profiles are visible. The hair may have been lost during the preparation of the specimen and not all hair follicles will contain hairs. Although it is often possible to see the attachment of the arrector pili muscle into the hair follicle or the papillary layer of the dermis, both attachments are hardly ever visible in the same section.

Draw a hair follicle at low magnification. Try to draw a composite from several hair follicles and associated structures, which captures their appearance from the bulb to the epidermis.

Sebaceous Glands

Sebaceous glands empty their secretory product into the upper parts of the hair follicles. They are therefore found in parts of the skin where hair is present. The hair follicle and its associated sebaceous gland form a pilosebaceous unit.

Sebaceous glands are also found in some of the areas where no hair is present, for example, lips, oral surfaces of the cheeks and external genitalia.

Sebaceous glands are as a rule simple and branched (Remember the nomenclature of glands!). The secretory portion consists of alveoli. Basal cells in the outermost layer of the alveolus are flattened. Basal cells are mitotically active. Some of the new cells will replenish the pool of basal cells, while the remaining cells are displaced towards the centre of the alveolus as more cells are generated by the basal cells. The secretory cells will gradually accumulate lipids and grow in size. Finally their nuclei disintegrate, and the cells rupture. The resulting secretory product of lipids and the constituents of the disintegrating cell is a holocrine secretion.

The lipid secretion of the sebaceous glands has no softening effect on the skin, and it has only very limited antibacterial and antifungal activity. Its importance in humans is unclear. Clinically the sebaceous glands are important in that they are liable to infections (e.g. with the development of acne).

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