Integumentary system

The integumentary system consists of the integument (Latin, covering) and its derivatives. It is the largest organ of the human body, 15-20% of total mass, made up of multiple layers of epithelial tissue that guard underlying muscles and organs. Skin pigmentation varies among populations, and skin type can range from dry skin to oily skin.
The adjective **cutaneous** literally means "of the skin" (from Latin *cutis*, skin).

Functions

1. **Protection:** an anatomical barrier between the internal and external environment in bodily defense; Langerhans cells in the skin are part of the adaptive immune system
2. **Sensation:** contains a variety of nerve endings that react to heat and cold, touch, pressure, vibration, and tissue injury.
3. **Heat regulation:** the skin contains a blood supply far greater than its requirements which allows precise control of energy loss by radiation, convection and conduction. Dilated blood vessels increase perfusion and heat loss while constricted vessels greatly reduce cutaneous blood flow and conserve heat.
4. **Control of evaporation:** the skin provides a relatively dry and impermeable barrier to fluid loss. Loss of this function contributes to the massive fluid loss in burns.
5. **Aesthetics and communication:** others see our skin and can assess our mood, physical state and attractiveness.
6. **Storage and synthesis:** acts as a storage center for lipids and water, as well as a means of synthesis of vitamin D by action of UV on certain parts of the skin.
7. **Excretion:** sweat contains urea, however its concentration is 1/130th that of urine, hence excretion by sweating is at most a secondary function.
8. **Absorption**: Oxygen, nitrogen and carbon dioxide can diffuse into the epidermis in small amounts, some animals using their skin for their sole respiration organ. In addition, medicine can be administered through the skin, by ointments or by means of adhesive patch, such as the nicotine patch or iontophoresis. The skin is an important site of transport in many other organisms.

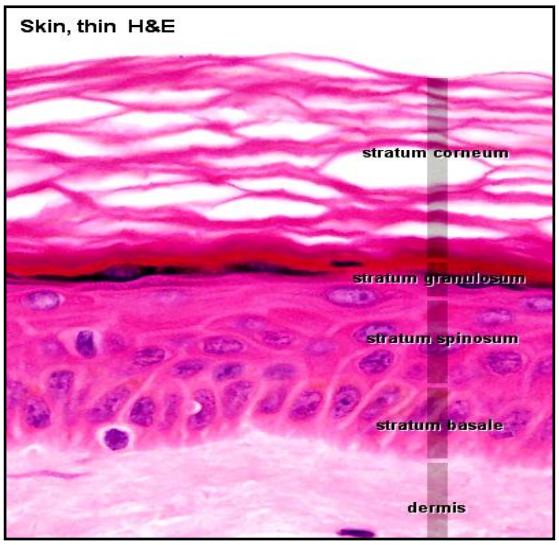
Skin is composed of three primary layers: the ***epidermis,*** which provides waterproofing and serves as a barrier to infection; the ***dermis,*** which serves as a location for the appendages of skin; and the ***hypodermis*** (subcutaneous adipose layer).
The thickness of the skin varies from less than 1mm to more than 5mm.

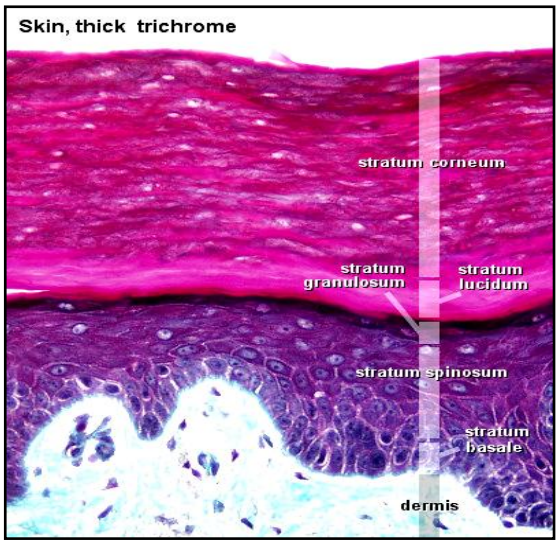
Thick skin (hairless skin) contains thick epidermis e.g **palms** of hands **soles** of feet. It has sweat glands, no hair follicles and no sebaceous glands.

Thin skin (thin epidermis) contains hair follicles, sweat glands and sebaceous glands.
The terms thick skin and thin skin are **misnomers** refer only to the thickness of the epidermis. The **thickest** skin is found in the upper portion of the **back** where the dermis is very thick. In contrast, in the **eye lid** the skin is very **thin**.

Epidermis

The epidermis is the outer avascular epithelial layer. It is consists of a **keratinized stratified squamous epithelium**. Epidermis is composed predominantly of **keratenocytes** (held together by **desmosomes**) and it is divided into several **layers** where cells are formed through mitosis at the innermost layers. They move up the strata (layers) changing shape and composition as they differentiate and become filled with **keratin** (a tough, fibrous protein). They eventually reach the top layer called stratum corneum and become **sloughed off**, or **desquamated**. This process is called **keratinization** and takes place within **weeks**. The outermost layer of epidermis consists of 25 to 30 layers of dead cells.





Sub-layers of epidermis
Epidermis is divided into five distinct layers beginning with the deepest

The **stratum germinativum** (also **stratum basale** or **basal cell layer**) is the layer of keratinocytes that lies at the base of the epidermis immediately above the dermis. It consists of a **single layer** of tall, **simple cuboidal to low columnar** epithelial cells lying on a **basement membrane** with less cytoplasm (basophilic) than the cells above and have closely spaced nuclei. These cells undergo rapid cell division, mitosis, and start to migrate **upward** to replenish the regular loss of skin by shedding from the surface. Each cell has numerous free ribosomes, small Golgi complex, mitochonderia and rER with **scattered intermediat filaments** (the essential protein in keratin production). About 25% of the cells are **melanocytes**, which produce melanin, which provides pigmentation for skin and hair. Basal cell carcinoma originates in this layer.

The **stratum spinosum** is a **multi-layered** arrangement of **cuboidal** cells that sits beneath the stratum granulosum. Adjacent cells are joined by **desmosomes**, giving them a **spiny** appearance (it is called **prickle cell layer**) to provide structural **support**, helping the skin resist **abrasion**. Cells of the stratum spinosum actively synthesize **intermediate filaments** (could be visualized by **light microscope**) called **cytokeratins**, which are composed of keratin.

The **stratum granulosum** layer typically contains **1 to 3 rows** of **squamous** cells with many small basophilic granules in their cytoplasm **(keratohyalin granules)**. As the number of granules increases they converted into intracellular protein keratin, which is called **soft keratin,** in contrast to the hard keratin of hair and nail. The lamellar granules are **exocytosed** in this layer to generate a waterproof barrier. This layer also includes **lamellar granules** and **tonofibrils**.

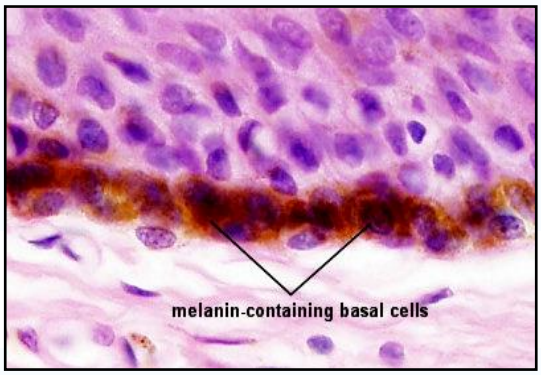
The **stratum lucidum** (Latin for "clear layer") is a thin, clear layer of **dead** skin cells in the epidermis, and is named for its translucent appearance under a microscope, only found on the **thick skin**, with **non nucleated** cells and **immature keratin**. It is considered by some histologists as a subdivision of the stratum corneum.

The **stratum corneum** ("horny layer") is the outermost layer of the epidermis (the outermost layer of the skin). It is composed mainly of **dead squamous** cells that **lack nuclei** and filled with **keratin**. As these dead cells slough off, they are continuously replaced by new cells. In the human forearm, for example, about 1300 cells/cm^2/hr are shed and commonly accumulate as **house dust**. Cells of the stratum corneum contain keratin, a protein that helps keep the skin **hydrated** by **preventing** water **evaporation**. In addition, these cells can also **absorb** water, further aiding in hydration and explaining why humans and other animals experience wrinkling of the skin on the fingers and toes (colloquially called "**pruning**") when immersed in water for prolonged periods.
The thickness of the stratum corneum varies according to the amount of protection and/or grip required by a region of the body, being thickest in thick skin. When subjected to unusual amount of friction it becomes thicker e.g ***calluses*** of the palm and finger tips. In general, the stratum corneum contains 15 to 20 layers of dead cells.
Other cells of the epidermis include
1. Melanocytes 2. Langerhans cells 3. Merckle cells

Melanocytes

The brown colour component of skin is due to ***melanin***, which is produced in the skin itself in cells called melanocytes (typically 1000-2000cell / sqr. mm; **1:4-1:10** of keratinocytes). Melanocytes are **ectodermal** in origin, derived exclusively from the neural crest. These cells are located in the epidermis (**basal layer**) and send fine **processes** (**dendrites**) between the other cells (**no desmosomes** with keratinocytes). In the melanocytes, the melanin is located in **membrane-bound inclusions** 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.These cells produce melanin (**melanogenesis**), which is a pigment found in the skin, eyes, and hair.

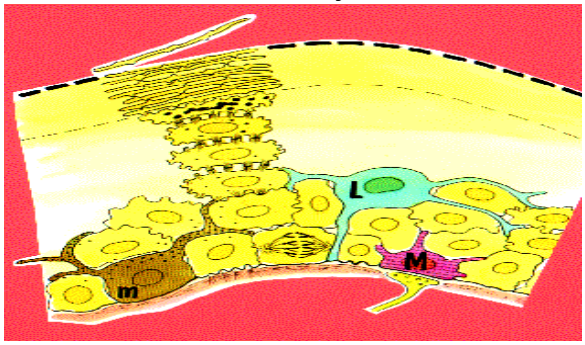
Melanocytes can transfer melanin to keratinocytes - mainly to the basal cells. The fine processes of melanocytes may invade keratinocytes and bud-off part of the melanocyte cytoplasm, including the melanosomes, within the keratinocytes. Melanin protects the chromosomes of mitotically active basal cells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



Melanogenesis is under the effect of

1. **Race**, there are both **basal** and **activated** levels of melanogenesis; lighter-skinned people generally have low basal levels of melanogenesis. The difference in skin color between fair people and dark people is due **not** to the number **(quantity**) of melanocytes in their skin, but to the melanocytes' level of **activity.**
2. **Light,** exposure to UV radiation generally causes increased melanogenesis, to protect the DNA of the keratinocytes from radiation
3. **Hormones**, 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.
4. **Age,** with aging melanocytes fail to produce melanin e.g hair turns white

Albinism is a **recessive hereditary** condition in which the melanocytes do not produce melanin (lack **tyrosinase** enzyme). People appear very pale, and, depending on the type of albinism, will also have lack of pigment in the iris of the eye, causing them to appear pink or violet due to visibility of the underlying blood vessels. In the most commonly-inherited form of albinism, the eyes are blue.



Langerhans' cells

Langerhans' cells are dendritic cells abundant in epidermis, containing large granules called **Birbeck granules**, 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 (**no desmosomes**) 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.

Merkel cells

Merkel cells are large **oval** cells found in the skin of vertebrates. They possess numerous cytoplasmic **granules**, typical of polypeptide-secreting endocrine cells. These cells are commonly associated with free **nerve endings** and located among the cells of the **germinativium**. The function of Merkel cells is still **not** fully established, though it is thought they may function as **sensory mechanoreceptors** or produce local **neuroendocrine** secretions. It is believed that they belong to the diffuse neuroendocrine system of the body.

Changes in Human Skin Color

1. Tanning Effect – see comments concerning light exposure and the action of melanocytes.
2. Reddening of skin occurs due to an increased blood flow in the underlying dermis. The increased blood flow may be caused by:

    a. The release of the vasoactive chemical Histamine due to trauma in the skin (inflammation).
    b. An increase in body temperature which leads to a vasodilatation of blood vessels in the dermis.
    c. Strong emotional states will lead to an increase in blood flow in the dermis.

3. Blanching of Skin ("turning pale") occurs due to decreased blood flow to the skin. This decreased blood flow may be caused by:

    a. A sudden drop in blood pressure – shock.
    b. Hypothermia
    c. Emotional states – fear, panic.

4. Cyanosis – bluish color in skin due to sustained reduction in blood supply to the skin. Hemoglobin in blood becomes depleted of oxygen and appears blue through the layers of skin.

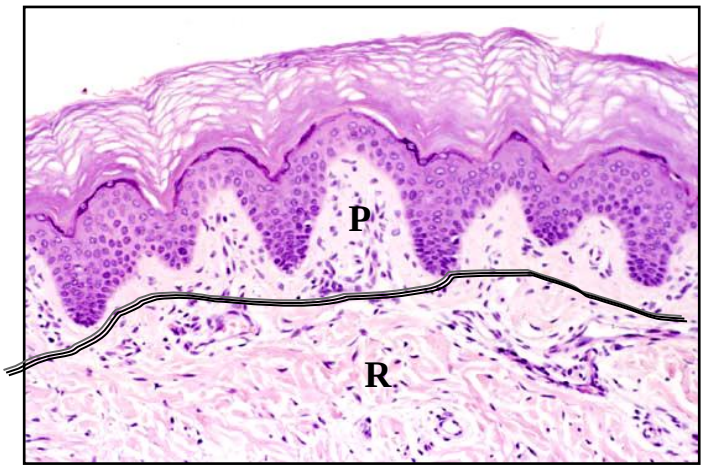
5. Jaundice – When liver function is interrupted due to cirrhosis, liver cancer or blockage of bile flow, yellow bile pigments and bilirubin accumulate in the skin and whites of the eyes.

6. Tumor of the pituitary gland or Addison’s disease leads to an over production of melanocyte stimulating hormone (MSH). MSH darkens the skin.

7. Vitiligo – In this condition an individual loses their melanocytes. It is thought to be due to an autoimmune disease in which the immune system mistakenly attacks and destroys the body’s melanocytes.

Dermis

The **dermis** is the layer of skin beneath the epidermis that consists of connective tissue and cushions the body from stress and strain (1-2mm thick). The dermis is tightly connected to the epidermis by a **basement membrane**. It also harbors many nerve endings that provide the sense of touch and heat. It contains the hair follicles, sweat glands, sebaceous glands, apocrine glands, lymphatic vessels and blood vessels. The blood vessels in the dermis provide nourishment and waste removal to its own cells as well as the Stratum basale of the epidermis.
The dermis is structurally divided into two areas: a superficial area adjacent to the epidermis, called the ***papillary region***, and a deep thicker area known as the ***reticular region***.



Papillary region

The papillary region is composed of **loose areolar CT**. It is named for its fingerlike projections called *papillae* that extend toward the epidermis. The papillae provide the dermis with a "bumpy" surface that **interdigitates** with the epidermis, strengthening the connection between the two layers of skin. The dermis is **very well-vascularized**. Up to 4.5% of total blood volume is found in the dermis. The dermis has many **arterio-venous anastomoses**, which are important in **thermoregulation** of the body.

In the palms, fingers, soles, and toes, the influence of the papillae projecting into the epidermis forms contours in the skin's surface. These are called ***friction ridges***, because they help the hand or foot to grasp by increasing friction. Friction ridges occur in patterns (**fingerprint**) that are genetically and epigenitically determined and are therefore unique to the individual, making it possible to use fingerprints or footprints as a means of identification.

Reticular region
The reticular region lies deep in the papillary region and is usually much **thicker**. It is composed of **dense irregular connective tissue**, and receives its name from the dense concentration of **collagenous, elastic,** and **reticular** fibers that weave throughout it. These protein fibers give the dermis its properties of strength, extensibility, and elasticity. With aging the collagen fibers thicken and cross-link

and the elastic fibers lose much of their elasticity, causing increased **wrinkling** of the skin. Also located within the reticular region are the roots of the hair, sebaceous glands, sweat glands, receptors, nails, and blood vessels.

The **hypodermis** (superficial facia) is not part of the skin, and lies below the dermis. Its purpose is to attach the skin to underlying bone and muscle as well as supplying it with blood vessels and nerves. It consists of loose connective tissue and elastin. The main cell types are fibroblasts, macrophages and adipocytes (the hypodermis contains 50% of body fat). Fat serves as padding and **insulation** for the body (thick in cold climate).

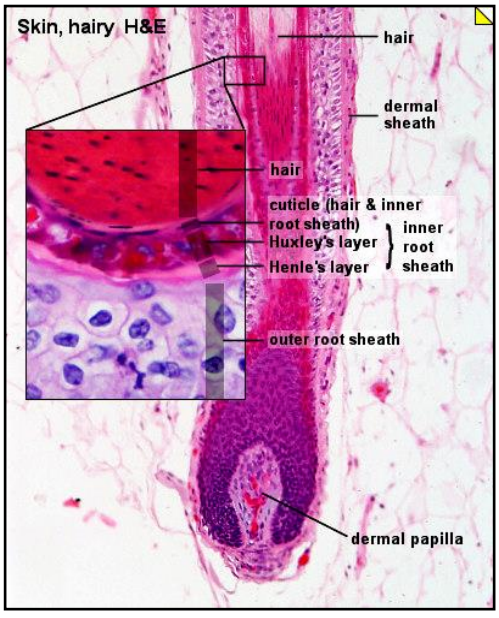
Appendages of the Skin

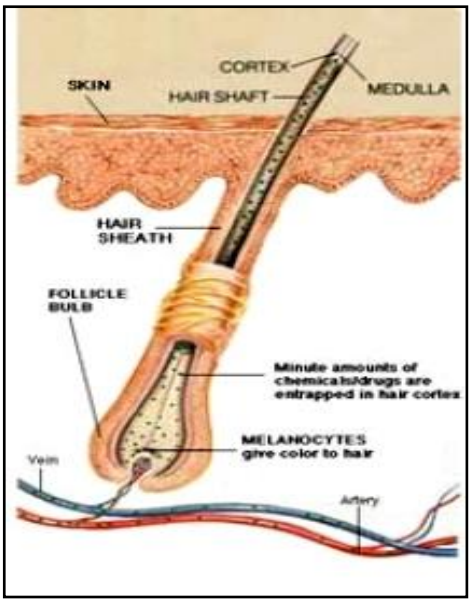
Hair

Hairs are one of the unique characteristics of mammals. They are thin filaments of **keratin** (hard keratin) that develop in the dermis from **epithelial invaginations** of the epidermis. Hairs are found on skin of most parts of the body, apart from thick skin**.**

The appearance of hairs (length, thickness, pigmentation, density) depends on many factors including: age, race, sex, hormones, and location on the skin. Hairs grow **discontinuously**, with periods of **growth** followed by periods of **inactivity**.

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 keratinize 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.

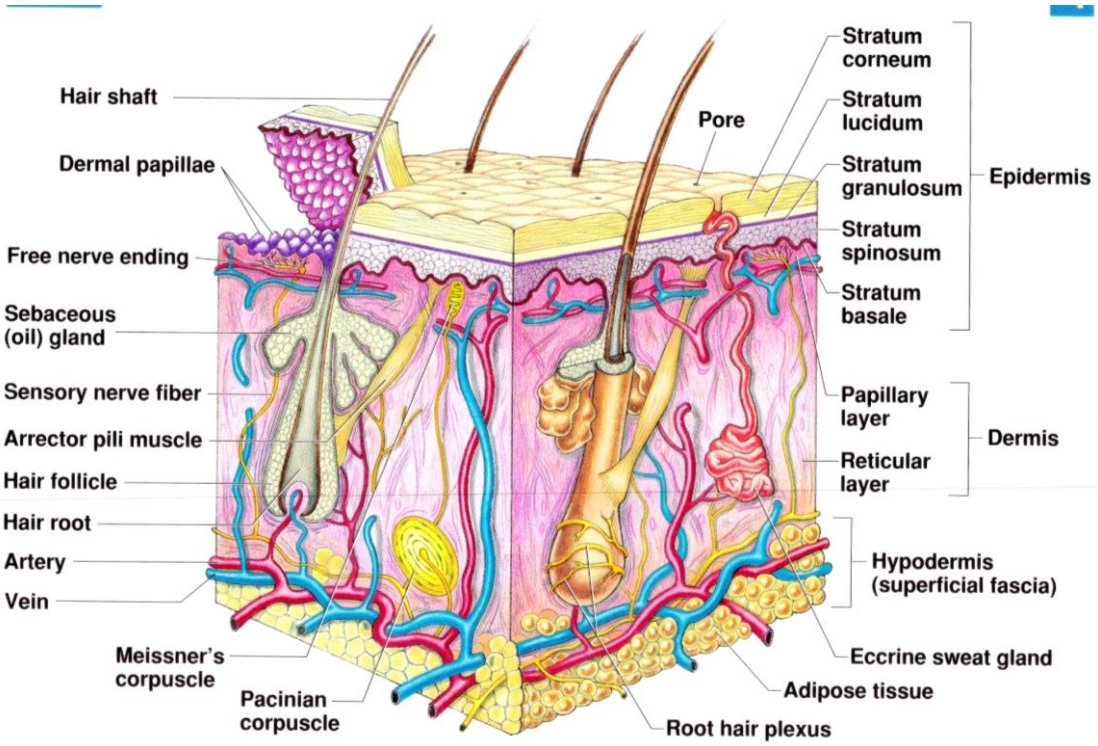




Sebaceous glands

The sebaceous glands are **dermal exocrine glands** associated with hairs and which secrete an oily substance (**sebum**) on the growing hair. The sebum is important in maintaining the **flexibility** of the hair. The glands are composed of alveoli and a short secretory duct. The outermost cells of the gland are filled with lipid droplets. These cells are secreted in their entirety (**holocrine secretion**).The extrusion of the sebum results from the contraction of the arrector pili muscles. The sebum secretion is influenced by **sex hormones** (androgens and estrogens) and during hormonal imbalance during puberty may result in adolescent **acne**. Sebaceous glands are **not** present in thick skin.

*[**Holocrine** secretions are produced within the cell followed by the rupture of the plasma membrane, thus releasing the cellular contents into the lumen e.g meibomian glands of the eyelid.]*



Sweat glands

These are simple exocrine glands that secrete **sweat**. The secretory units are **simple convoluted tubular** epithelial structures in the dermis and a straight secretory duct. The convolutions of the secretory unit are seen in histological preparations as many associated profiles of the same unit. The secretory ducts are surrounded by **myoepithelial cells**, which on contraction cause the expulsion of the sweat.

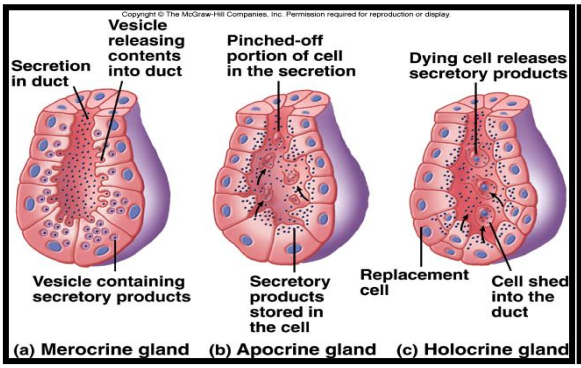
Two types of sweat glands are found:

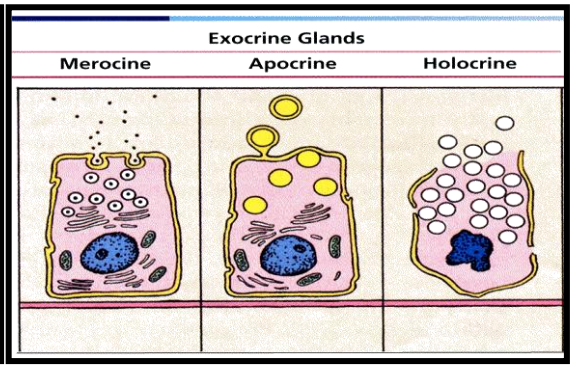
- **Eccrine sweat glands** (**Merocrine** sweat glands) these are found **all over** the body including the thick skin. They are coiled tubular glands derived from the outer layer of skin but extending into the inner layer used for **body temperature regulation.** They produce a clear, odorless substance, consisting primarily of **water and NaCl**. The eccrine sweat glands have **cholinergic innervation.**

*[A cell is classified as **merocrine** if the secretions of that cell are excreted via exocytosis from secretory vesicles opening into a gland's acinus and flowing through an epithelial-walled duct or ducts and thence onto a bodily surface or into the lumen. Merocrine is the most common manner of secretion. The gland releases its product and no part of the gland is lost or damaged e.g salivary glands]*

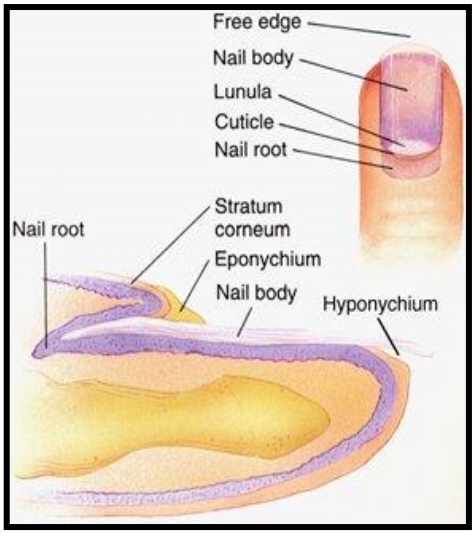
- **Apocrine sweat glands** these are **large** sweat glands located in the **axilla** (armpit) and also in association with the **external genitalia** and **anus**. They have very large secretory units and **myoepithelial cells**, in which the apical part of the secretory cells including their contents, are secreted into the lumen (apocrine secretion). Apocrine sweat is a **milky**, **proteinaceous** and **odourless** secretion. The breakdown of this secretion **by bacteria** is the cause of the typical **smell** of sweat from the armpits. The apocrine sweat glands only become **functional** at **puberty** and are influenced by sex steroids. The apocrine sweat glands have **adrenergic innervation.**

*[Cells which are classified as **apocrine** bud their secretions off through the plasma membrane producing membrane bound vesicles (pinching of part of the cell) in the lumen e.g mammary glands.]*





Nails

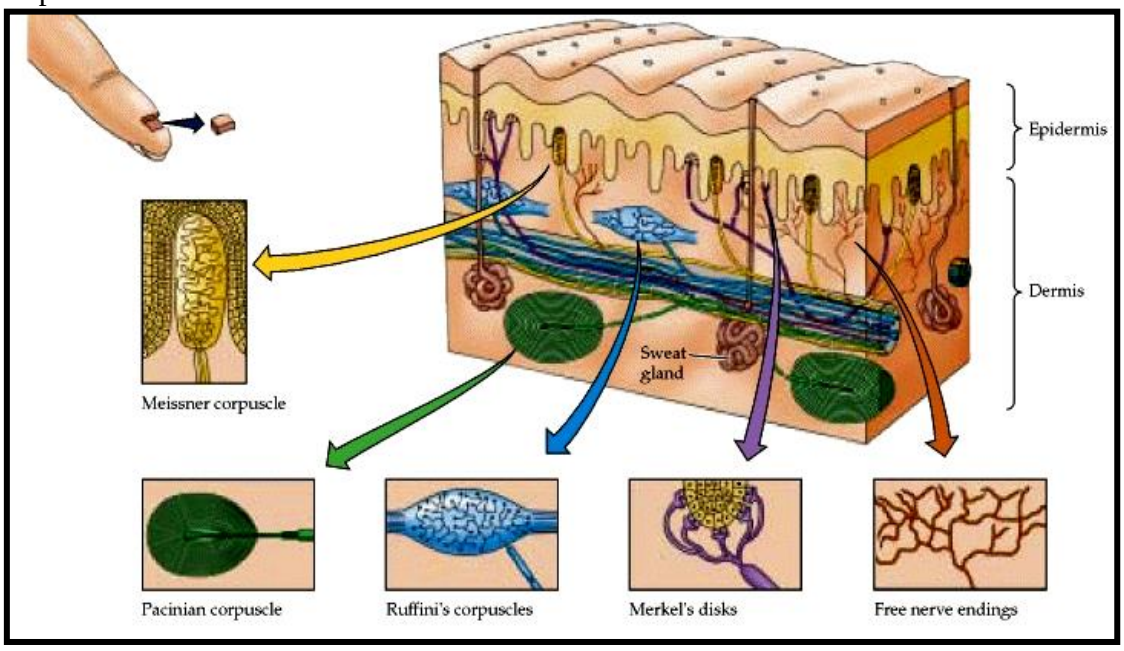


Nails are horny plates of keratin on the dorsal surface of the terminal phalanges of the hand and foot (fingers and toes). The **nail plate** (nail body) is composed of tough, hard, clear non-desquamating keratin, which sits on the **nail bed**, composed of a layer of epidermal cells. Surrounding the nail is the **nail groove**. The formation of the nail and its keratin occurs in the **nail root**. This region shows many mitoses of the epithelial cells. These germinative cells of the nail root are known as the **dorsal** and **ventral matrix**. Part of the ventral matrix (seen as a

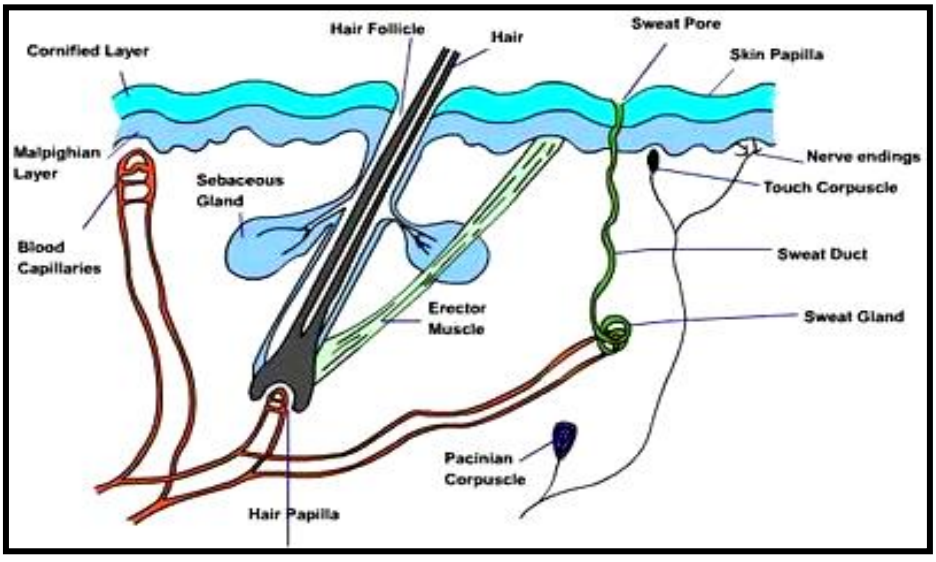
whitish half-moon near the dorsal nail groove) is the **lunula**. The keratin above the nail groove is thickened (**eponychium** or **cuticle**). Below the nail, near its free surface, the keratin is also thickened (**hyponychium**).

Nerve supply

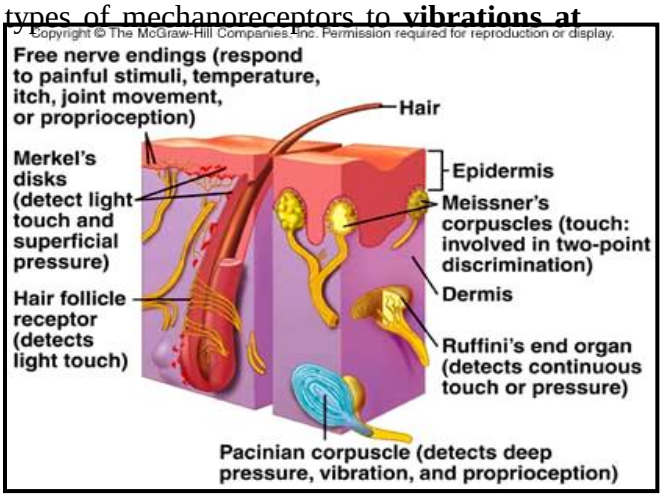
The integument is richly innervated with both motor and sensory modalities. Autonomic motor nerve endings provide innervations to the numerous 1) glands and 2) smooth muscle of the blood vessels and arrector pili. Peripheral terminals of sensory nerves provide information about the environment to the organisms. The sensory nerve terminals are classified as either **encapsulated** (invested by CT and/or Schwann cells) or **free**. However, in both types of terminals the nerve endings loose their myelin sheath. **Encapsulated terminals** include tactile (Meissner's) corpuscles, bulboid corpuscles (Krause's end bulb), lamellar (Pacinian) corpuscles, and Ruffini's corpuscles. **Free** terminals include free endings, Merkel's disc and hair follicle receptors.



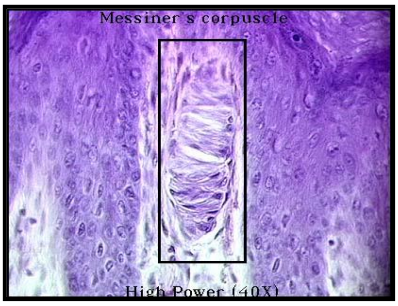
- **Free nerve endings** are **non-encapsulated** nerve endings in the **epidermis** and these receptors sense **pain and temperature**. Free nerve endings have **no complex** sensory structures, unlike those found in Meissner's or Pacinian corpuscles. They loose their myelin sheath at the epidermal / dermal junction and **pass** into the **epidermis**

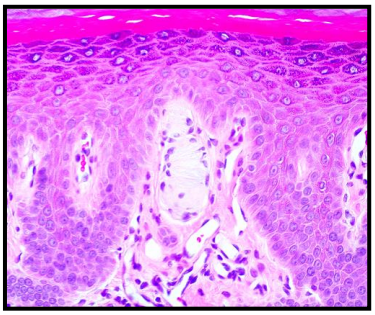


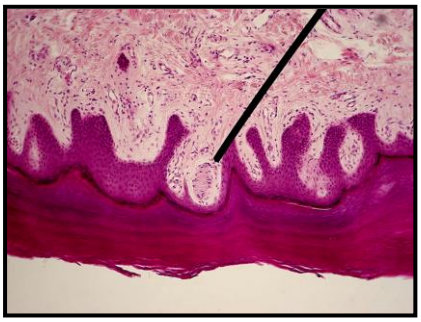
- **Merkel disk receptor** are **non- encapsulated** mechanoreceptors surrounding hair follicles and responsive to **touch**. Merkel nerve endings have a wide distribution. Merkel nerve endings are found in the **basal layer**. They are the **most sensitive** of the four main types of mechanoreceptors to **vibrations at low frequencies**
- **Hair follicle receptors** these mechanoreceptors sense the presence and direction of hair displacement.



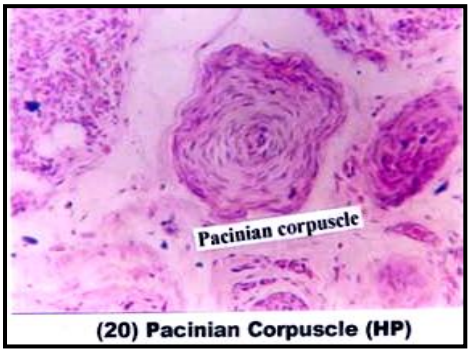
- **Meissner corpuscles** (or **tactile corpuscles**) are mechanoreceptors present in the **dermal papilla**. They are a type of **encapsulated** nerve ending in the skin that is responsible for sensitivity to **light touch** (sensitive to **low frequency** stimuli). Also, Meissner's corpuscles **do not** detect pain; this is signalled exclusively by free nerve endings. The number of Meissner corpuscles per square millimeter of human skin on the fingertips drops with age



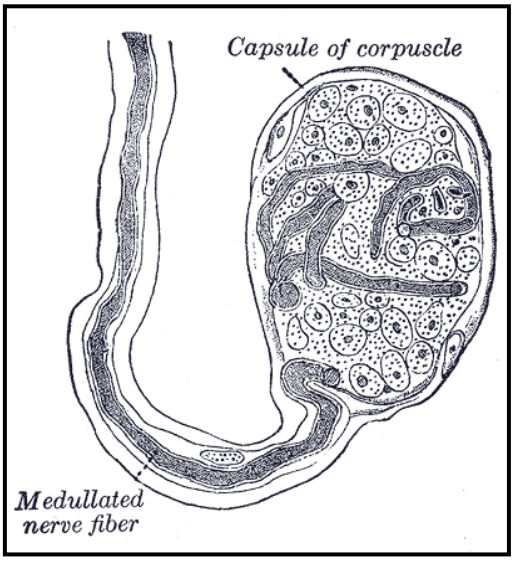




- **Pacinian corpuscles** are found in the **dermis** of thick skin of fingers and respond to **pressure and vibration**. Pacinian corpuscles have a large **receptive field** on the skin's surface with an especially sensitive center. They only sense stimuli that occur within this field. Similar in physiology to the Meissner's corpuscle, Pacinian corpuscles are **larger and fewer** in number than both Merkel cells and Meissner's corpuscle.



- **Krause end bulb**s (**bulboid corpuscles)** are found in the dermis and respond to **cold** and low-frequency vibration. These encapsulated mechanoreceptors are found in the papillary layer of the **dermis** and in the epithelium of the **oral mucosa** of the oral cavity and **tongue**.



- **Ruffini's corpuscles** – are encapsulated mechanoreceptors located deep in the reticular layer where they respond to **distortion or stretching** of the skin (sustained or **continuous** stress)