

INTEGUMENTARY SYSTEM

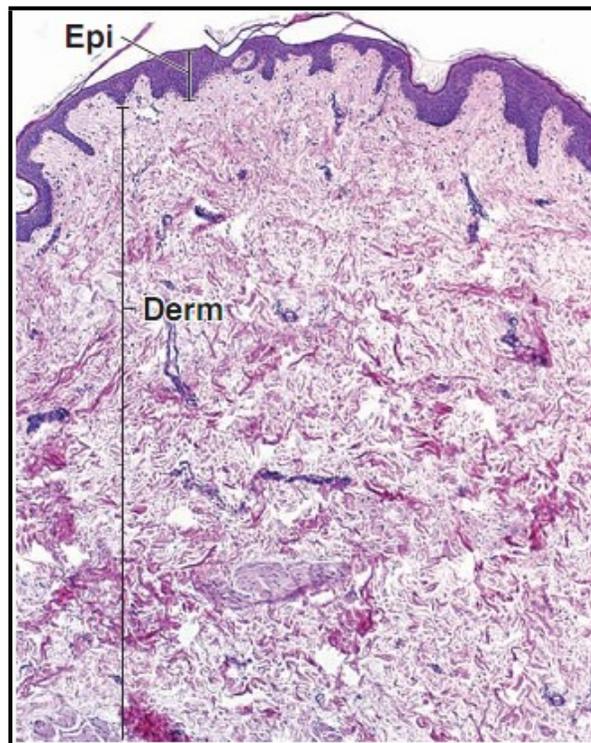
Skin and its derivatives constitute integumentary system. The skin forms external covering of body and is largest organ. It consists of 2 layers:

- a. **Epidermis:** It is composed of keratinized stratified squamous epithelium that grows continuously but maintains its normal thickness by process of desquamation. *It is derived from ectoderm.*
- b. **Dermis:** It is composed of dense connective tissue that imparts mechanical support, strength and thickness to the skin. *Dermis is derived from mesoderm.*

Below dermis is *hypodermis* which contains variable amount of adipose tissue arranged into lobules separated by CT septa. It lies deep to dermis and is equivalent to sub-cutaneous fascia described in gross anatomy.

Epidermal derivatives of skin:

- Hair and hair follicles
- Sweat glands, Sebaceous glands
- Nails
- Mammary glands



Functions of skin:

1. Act as barrier that protects against physical, chemical and biological agents in external environment
2. Conveys sensory information about external environment to nervous system
3. Play role in thermoregulation. Sweat glands and dilated blood vessels aid heat loss, while constricted vessels greatly reduce blood flow and conserve heat

4. Control of evaporation. Skin provides relatively dry and semi-permeable barrier to reduce fluid loss
5. Act as storage centre for lipids and water
6. Absorption. O₂/N₂/CO₂ can diffuse into epidermis. Certain lipid-soluble substances may be absorbed through skin
7. Skin act as water resistant barrier so essential nutrients are not washed out of the body
8. Perform endocrine functions by secreting hormones, cytokines, growth factors and convert precursor molecules into hormonally active molecules (Vitamin D)

EPIDERMIS

It is composed of *stratified squamous epithelium* in which 4 distinct layers can be identified. In case of thick skin, 5th layer is observed. These layers are:

1. **Stratum Basale** (also called stratum germinativum)
2. **Stratum Spinosum:** It is also called spinous or prickle cell layer.
3. **Stratum Granulosum**
4. **Stratum Lucidum:** This layer is limited to thick skin
5. **Stratum Corneum:** This layer is composed of keratinized cells

Malphigian Layer: Stratum basale + Stratum spinosum

Stratum Basale

It is *lowermost layer* and represented by single layer of cells that rest on basal lamina. It *contains stem cells* from which new cells, keratinocytes, arise by mitotic division. For this reason, stratum basale is also called *stratum germinativum*. Cells are small and are *cuboidal to low columnar*. Cells have *less cytoplasm*; their nuclei are more closely spaced. Basal cells also contain various amount of melanin in their cytoplasm. Cells exhibit *extensive cell junction*; they are connected to each other, to keratinocytes and cells of stratum spinosum by desmosomes and to underlying basal lamina by hemi-desmosomes. As new keratinocytes arise in this layer by mitotic division, they move into next layer, thus beginning their process of upward migration. This process terminates when cell becomes a mature keratinized cell, which is eventually sloughed off at skin surface.

Stratum Spinosum

It is several layers thick. Cells are larger than those of stratum basale. *Cells are polyhedral*. They exhibit numerous cytoplasmic processes or spines, which gives this layer its name. The processes are attached to similar processes of adjacent cells by desmosomes. The processes are very conspicuous because cells shrink during preparation and result in large intercellular spaces. Spiny appearance is due to shrinkage of cytoplasm between desmosomal attachments and wherever cells remain attached, small spiny processes radiate from surface of cells. Thus this layer is called spiny layer. These spiny processes contain cytokeratin filaments called Tonofilaments.

Stratum Granulosum

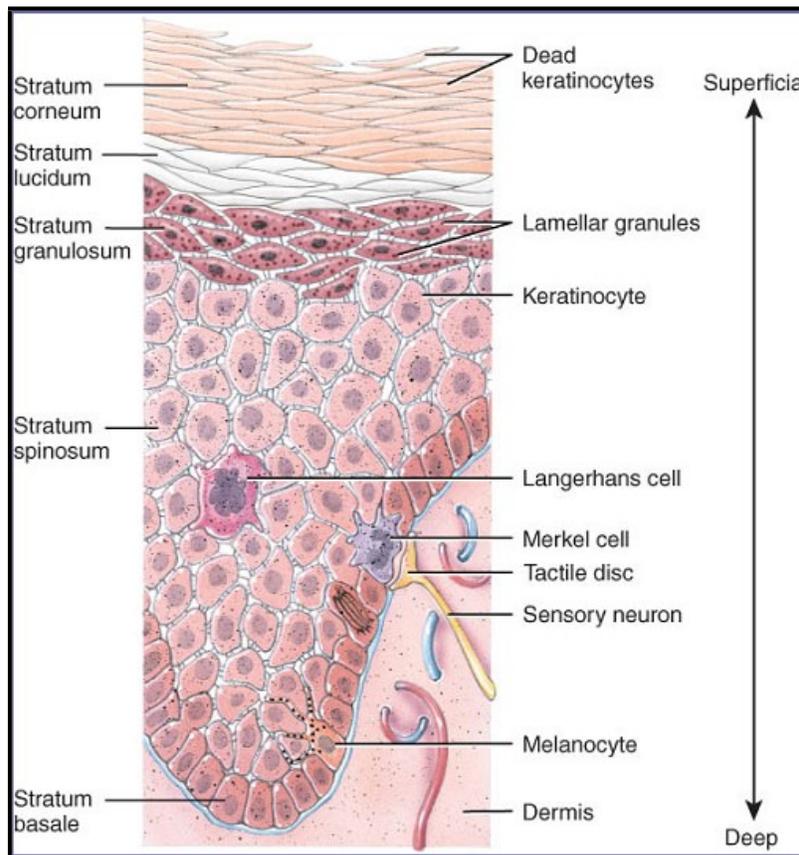
It is most superficial layer of non-keratinized portion of epidermis. **Keratinization begins here.** This layer varies from 1 – 3 cells thick. Cells are flattened lying parallel to dermal – epidermal junction. The cells contain “*keratohyaline granules*”. These granules contain cystine – rich and histidine – rich protein *profilaggrin*. It is precursor of filaggrin (play role in keratinization). This layer has presence of *lamellar granules*. These granules contain lipid and enzymes. This forms hydrophobic lipid envelop responsible for skin’s barrier properties.

Stratum Lucidum

This layer is present in thick skin and hairless regions. This layer is thin, clear layer of dead skin cells. Layer has presence of flattened keratinocytes filled with protein *eleidin*.

Stratum Corneum

It is outermost, thickest layer. It is about 20 – 30 cells thick. Cells lose their nucleus and cytoplasmic organelles and become filled almost entirely with keratin filaments. Thick plasma membrane of cells is coated from outside with layer of lipid that form major constituent of water barrier in epidermis.



DERMIS

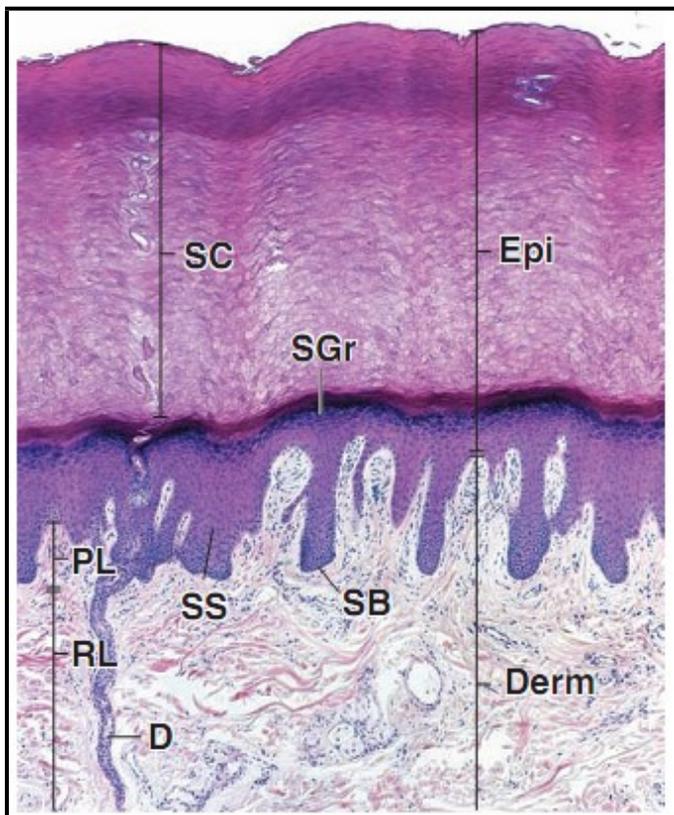
It is integrated system of fibrous/filamentous and amorphous CT that accommodates nerves/blood vessels/epidermally derived appendages. Major cells are ***fibrocytes, macrophages and mast cells***. Blood borne cells like lymphocytes, plasma cells enter dermis in response to

various stimuli. Dermis provides tensile strength and elasticity to skin through extra-cellular matrix composed of collagen fibrils. It harbors many nerve endings. Smooth muscle fibers are located near hair follicles and are called **arrector pili muscles**.

Constituent of dermis are Mesodermal in origin except nerves which like melanocytes are derived from neural crest. **Major component of dermis is collagen (Type I)**. Type IV collagen is present in basement membrane. Type VII collagen is present in anchoring fibrils.

Dermis is composed of 2 layers:

1. **Papillary layer:** It is superficial layer, thinnest layer and composed of loose CT. It is present just beneath epidermis. It protrudes into epidermis forming *dermal papilla*. When epidermis invaginates into dermis, *epidermal pegs* are formed.
2. **Reticular layer:** It lies deep to papillary layer. It is less cellular than papillary layer. It is thicker layer and consist of dense irregular CT. it contains mainly type I collagen and elastic fibers.



Photograph of skin showing different layers:

Epidermis (Epi), stratum corneum (SC), stratum granulosum (SGr), stratum spinosum (SS), stratum basale (SB), papillary layer (PL), reticular layer (RL), dermis (Derm) and ducts of sweat gland (D)

Dermal – Epidermal Junction: It is formed by a porous basement membrane zone. Basal keratinocytes are most important components. Dermal fibroblasts are also involved. **Mainly type IV collagen is present.** Basal lamina includes lamina lucida and lamina densa. Plasma membrane of basal cells is attached to basal lamina by hemi-desmosomes. 4 components of this junction are:

1. Cell membrane of basal cells
2. Lamina lucida
3. Lamina densa

4. Sub-basal lamina

Hypodermis: It is present beneath dermis. It is layer of loose CT. it is not part of skin but rather superficial fascia seen in gross anatomic dissections. This layer is also called *Panniculus adiposus*.

Cells of Epidermis

1. Keratinocytes
2. Non-keratinocytes
 - a. Melanocytes
 - b. Merkel's cells
 - c. Langerhan's cells

Melanocytes and Merkel's cells are derived from neural crest cells whereas Langerhan's cells are bone – marrow derived.

Keratinocytes

It is the predominate cell of epidermis. These cells originate from basal epidermal layer. On leaving this layer, keratinocytes assumes 2 essential activities:

- a. Produce keratin
- b. Form epidermal – water barrier

Keratohyaline granules are characteristic feature of stratum Granulosum. They contain 2 important intermediate filaments – associated protein, filaggrin and trichohyalin (in hairs). They initiate conversion of granular cells into cornified cells in process called keratinization. It involves:

- Breakdown of nucleus and organelles
- Thickening of plasma membrane

Finally cells are regularly exfoliated (desquamated) from surface of stratum corneum. Lamellar granules contents are mainly lipid in nature. Contents are released by exocytosis. The organization of these lipid is responsible for the formation of epidermal – water barrier.

Melanocytes

- Derived from neural crest cells. These are pigment synthesizing cell with spherical nucleus and present mainly in basal layer.
- Desmosomal attachments are absent. Hemidesmosomes are present
- Melanin is produced in membrane – bound organelle called *melanosomes*. Enzyme **tyrosinase** is needed to produce melanin. Tyrosinase enzymes is synthesized in RER and stored in Golgi complex.
- In H&E staining, they are seen in basal layer with *clear cytoplasm*

Tyrosin → 3, 4 – dihydroxyphenylalanine (DOPA) → Dopaquinone → Melanin

Langerhan's cells

- Bone marrow derived
- Called **skin macrophages**
- **Star shaped** with indented nucleus
- Desmosomes are absent

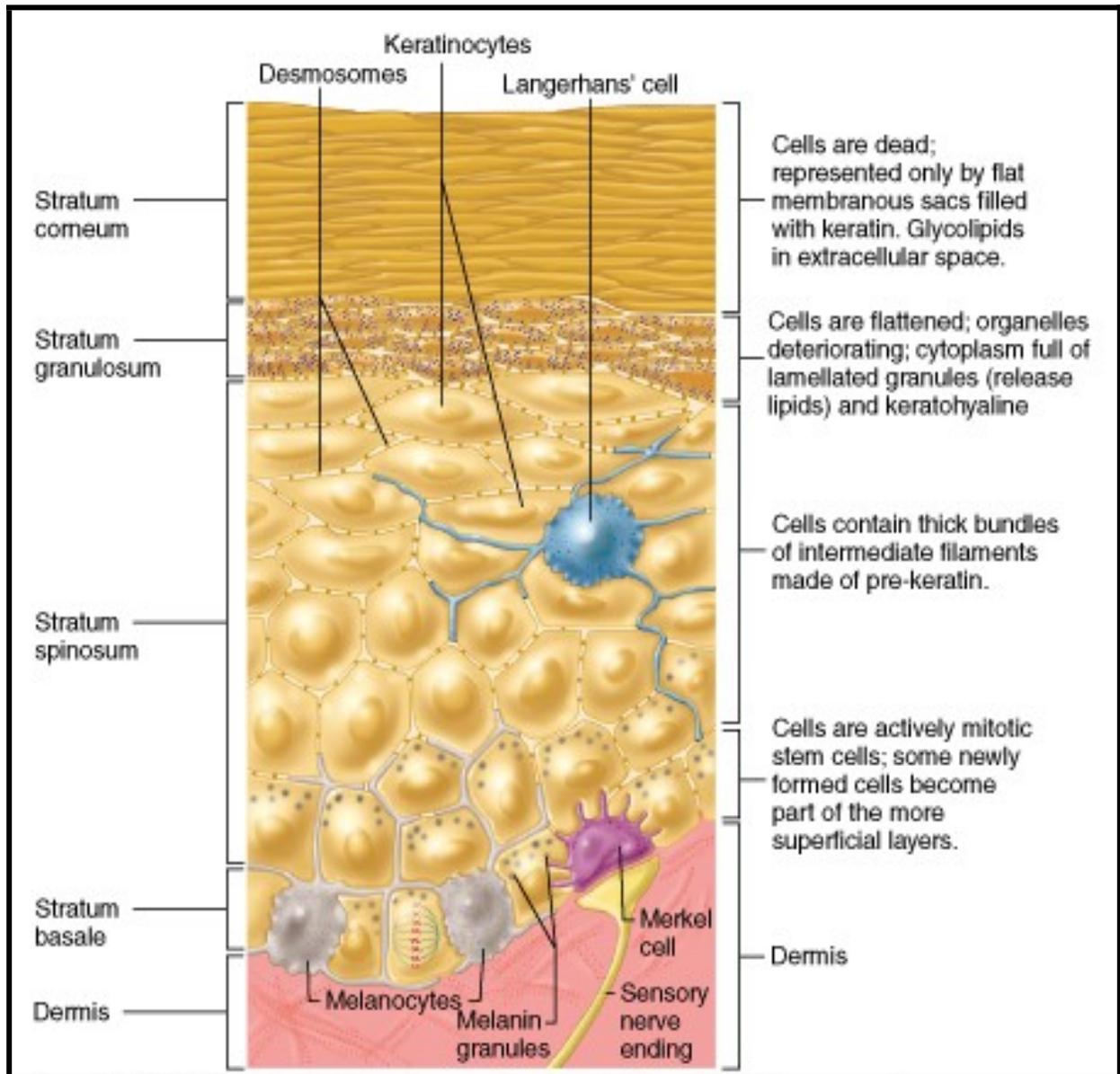
- Act as APC (Antigen Presenting Cells)
- Occurs mainly in stratum spinosum
- Involved in delayed type hypersensitivity

Merkel cells

- Derived from neural crest cells
- Called **tactile epitheloid cells**
- Located in basal region. Their long axis is usually parallel to surface of skin
- Nucleus is lobulated. Cytoplasm is clear and lack Tonofilaments
- Presence of desmosomes
- Associated with axon to form complex called *tactile hair disc*.
- Oval shaped cells

Cytoplasm of Merkle cell is denser than Melanocytes and Langerhan's cells

Melanocytes	Langerhan's cells	Merkel cells
Produce melanin	APC	Touch receptors, attached to nerve cells
Nucleus is spherical	Indented	Lobulated
Present mainly in basal layer	Stratum spinosum	Basal layer
Originate from neural crest cells	Bone marrow derived	Neural crest cells
Desmosomes absent	Absent	Present



Nerve supply

Small sub-cutaneous nerves give rise to a nerve plexus that provides the dermis and sends small branches to the epidermis. Several kinds of endings are present:

1. Free afferent nerve endings in epidermis & dermis (encircle follicle)
2. Free efferent nerve endings in hypodermis
3. Non-capsulated tactile corpuscles (Merkel's cells)
4. Encapsulated endings (Pacinian corpuscle/ Meissner's corpuscle)

Pacian corpuscles (Lamellar corpuscles) have been observed in the frog of an equine foot, the digital cushion of a dog/cat, and the anal sac wall of a cat. These are large ovoid structures found in the deeper dermis and hypodermis. These are deep **pressure receptors**. **Meissner's corpuscles** are localized within dermal papillae and serve as touch receptors.

Epidermal Skin Appendages:

Skin appendages are derived from down growths of epidermal epithelium during development. They include:

1. Hair follicles & their products (Hairs)
2. Sebaceous gland (produce sebum)
3. Eccrine sweat gland (sweat)
4. Apocrine sweat gland

Both hairs and sweat glands play specific roles in thermoregulation. Sebaceous glands secrete an oily substance that has protective functions. Apocrine gland produces serous secretion containing pheromones that act as sex attractant in animals. The epithelium of skin appendages can serve as a source of new epithelial cells for skin wound repair.

Hair follicles and Hair

Hair covers entire body except foot pads, hoofs, glans penis, musculo-cutaneous junctions, and teats of some species. **Hair** is flexible, keratinized structure produced by hair follicle. Part of hair above the surface of skin is called **hair shaft**. The part within follicle is **hair root**, which has terminal, hollow knob called **hair bulb**.

Shaft has 3 layers:

1. **Outermost cuticle:** It contains squamous cells that form outermost layer
2. **Cortex:** Contain densely packed keratinized cells (cuboidal). Desmosomes hold cells firmly together
3. **Medulla:** It forms central part of shaft and is loosely filled with cuboidal cells.

Hair follicle:

It is formed by growth of ectoderm into underlying mesoderm of embryo. Follicles are embedded in dermis, usually at an angle. Innermost layer, next to hair root is *internal epithelial root sheath*. It has 3 layers:

- a. **Internal root sheath cuticle:** It is formed by overlapping keratinized cells.
- b. **Middle granular epithelial layer (Huxley's layer):** It is composed of 1-3 layers of cells rich in trichohyaline granules (keratohyaline in hair)
- c. **Outer pale epithelial layer (Henle's layer):** It is composed of single layer of keratinized cells

External epithelial root sheath is composed of several layers of cells similar to epidermis. External to this is *glassy membrane* corresponding to basal lamina of epidermis. The entire epithelial root sheath is enclosed by **dermal root sheath** composed of collagen & elastic fibers.

Dermal papilla of hair follicle is region of CT directly underneath the hair matrix. Associated with most hair follicles are bundle of smooth muscles called **arrector pili muscles**. This muscle is attached to dermal root sheath and extends towards epidermis.

Sebaceous glands: Their secretory product is called **sebum**. It is oily secretion containing mixture of lipids and degenerating cells. These glands are most frequently associated with hair follicles. The sebaceous glands are connected to the hair follicle by short ducts lined by stratified squamous epithelium.

Sweat glands

Two types: Apocrine and Merocrine (Eccrine) glands

Apocrine gland is predominant sweat gland in domestic animals. They are distributed throughout the skin. In humans, they are mainly located in axillary, pubic and perianal region. The glands are simple saccular or tubular with coiled secretory portion and a straight duct **opening into adjacent hair follicles.**

Human **merocrine glands** (primary sweat gland) open independently of hair follicle. They are located in carnivore foot pad, frog of horses, carpal glands of swine, nasolabial region of ruminants. They are coiled simple tubular glands that open directly onto the skin surface rather than into the hair follicles. The secretory portion is composed of cuboidal epithelium with two distinct cell types. **The dark or mucoid cells** have more ribosomes and numerous droplets in the apical part of the cell. **The clear cells** lack cytoplasmic basophilia and they are believed to pump sodium ions into the gland lumen. The duct is straight and composed of two layers of cuboidal epithelial cells resting on a basement membrane. Myoepithelial cells form a discontinuous layer between the secretory cells and the basement membrane. Contraction of these cells expels sweat into the ducts.

Sweat glands serve both cooling and an excretory function. The secretory product is watery (serous) and slightly alkaline. **In horse, it is strongly alkaline.**

Glands of perianal region:

1. **Anal glands:** These are modified sweat glands occupying submucosa of columnar and intermediate zones of anal canal in dogs, cats, pigs. They open into anus. Carnivore anal glands secrete lipids; in pigs, it is mucoid substance.
2. **Anal sac glands:** These are diverticula lined by stratified squamous keratinized epithelium seen in carnivores. In dogs, only apocrine sweat glands; in cats both sweat and sebaceous glands are present.
3. **Circumanal glands:** These are sebaceous glands. Term **hepatoid** is used to describe glandular parenchyma because it resembles closely packed liver cells.

Other glands:

1. **Ceruminous glands (in external ear):** Modified apocrine sweat glands
2. **Tarsal glands in eye-lids** are sebaceous glands
3. **Ciliary glands in eye-lids** are apocrine sweat glands

Uropygial glands: These are also known as **oil or preen glands.** These are cutaneous glands in **birds.** It is well developed in aquatic species.

Mammary gland:

It is compound tubule-alveolar gland considered as modified sweat gland. Lipids are secreted by **apocrine method**; proteins & carbohydrates by **merocrine method.**

Mammary gland consists of udder and teats.

Actively lactating glands have much parenchyma and little connective tissue.

Lactating gland:

Secretory components are alveolar epithelial lining cells. Active cells are columnar. Lateral cell borders are usually indistinct.

Duct system:

1. One or two alveoli drain into **intra-lobular duct** lined by simple cuboidal epithelium.
2. It drains into non-secretory **lobular duct** lined by cuboidal or columnar epithelium.
3. It drains into **lobar duct** (Lactiferous duct). Many lobar ducts drain into **lactiferous sinus** (gland sinus), a common chamber at base of each quarter of udder.
4. It continues with **teat sinus** (teat cistern/ cavity of teat) which is lined by stratified cuboidal epithelium
5. Finally opens into **papillary ducts** (teat canal/streak canal) which open to external surface of teats.

Papillary duct:

Single in ruminants

2 in equines

2-3 in swines

4-7 in felines

7-16 in carnivores

Skin of teat is without hair follicles and sweat/sebaceous glands except **sheep & goat**.