หนึ่งอาจารย์หนึ่งผลงาน

ประจำปีการศึกษา 2551

เอกสารการบรรยาย

(PowerPoints)

วิชา 110203 Microscopic Anatomy

รองศาสตราจารย์ ดร. กรกช อินทราพิเชฐ

สาขาวิชาชีววิทยา

สำนักวิชาวิทยาศาสตร์

มหาวิทยาลัยเทคโนโลยีสุรนารี

สารบัญ

หัวข้อภาพเลื่อนการบรรยาย

บรรณานุกรม

PowerPoint

เรื่อง

Integument

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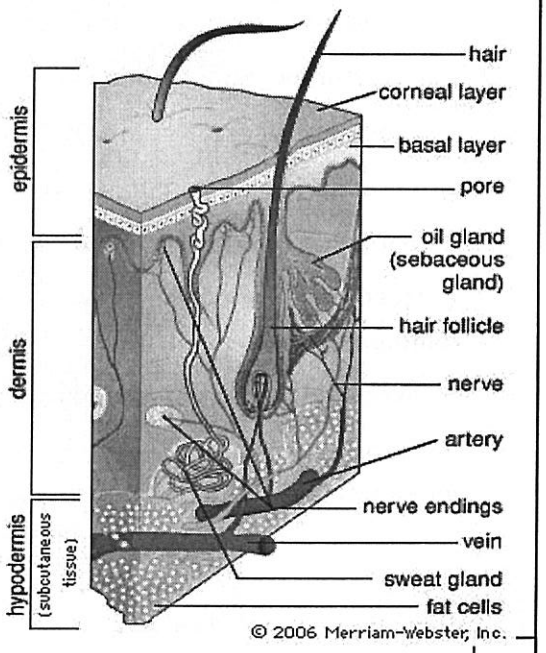
Integument

Integument

- The integument covers the body and protects the deeper tissues from injury, from drying and from invasion by foreign organisms. It contains the peripheral endings of many of the sensory nerves; it plays an important part in the regulation of the body temperature, and has also limited excretory and absorbing powers.
- Integument is the largest organ of the body, 16% of body weight.



Integument

- Integument become continuous with -
  - the mucous membranes of the digestive system at the lips and the anus,
  - the respiratory system in the nose, and
  - the urogenital systems where they surface.
- Additionally, the skin of the eyelids becomes continuous with the conjunctiva lining the anterior portion of the orbit.
- Skin also –
  - lines the external auditory meatus and
  - covers the external surface of the tympanic membrane.

Skin

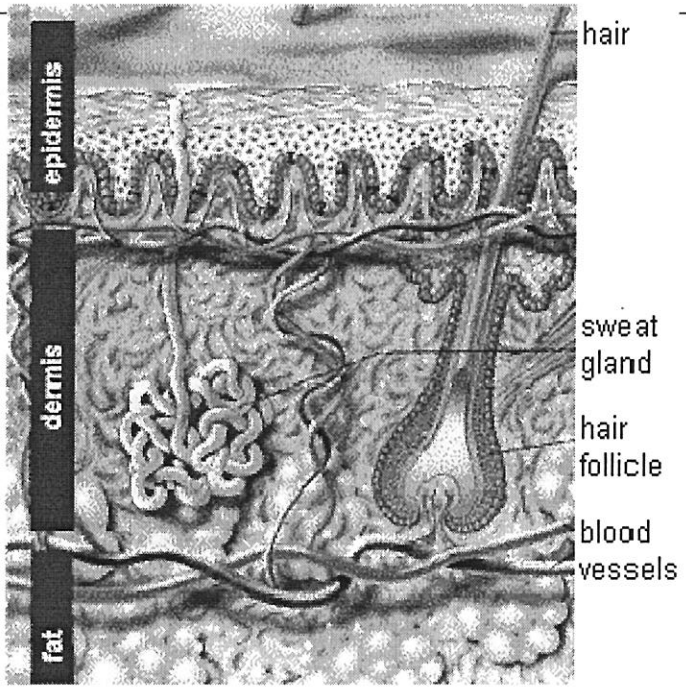
- Skin, the largest organ of the body.
- Skin performs many additional functions, including

1. providing a cover for the underlying soft tissues,
2. protection against injury, bacterial invasion, and desiccation;
3. regulation of body temperature;
4. reception of continual sensations from the environment (e.g., touch, temperature, and pain);
5. excretion from sweat glands; and
6. absorption of ultraviolet radiation from the sun for the synthesis of vitamin D that facilitates the uptake of calcium phosphate.

Skin - Epidermis

- Surface covering of the body that protects it and
- Receives external sensory stimuli,
- Consisting of an epidermis over a thicker dermis.
- The epidermis contains cells involved in
  - immune defenses,
  - sensory receptors,
  - pigment cells, and
  - keratin-producing cells.
- The last harden and migrate to the surface to form a dead, relatively dry outer layer of horny tissue that constantly sloughs away.

Skin



Skin - Dermis

- The dermis contains
  - sensory nerves and
  - blood vessels
  - connective tissue
  - hair
  - nail
  - sebaceous gland
  - sweat gland
- Collagen and elastin fibres give skin its tough, elastic quality.
- Cells scattered through it produce its components and take part in immune and other skin responses.

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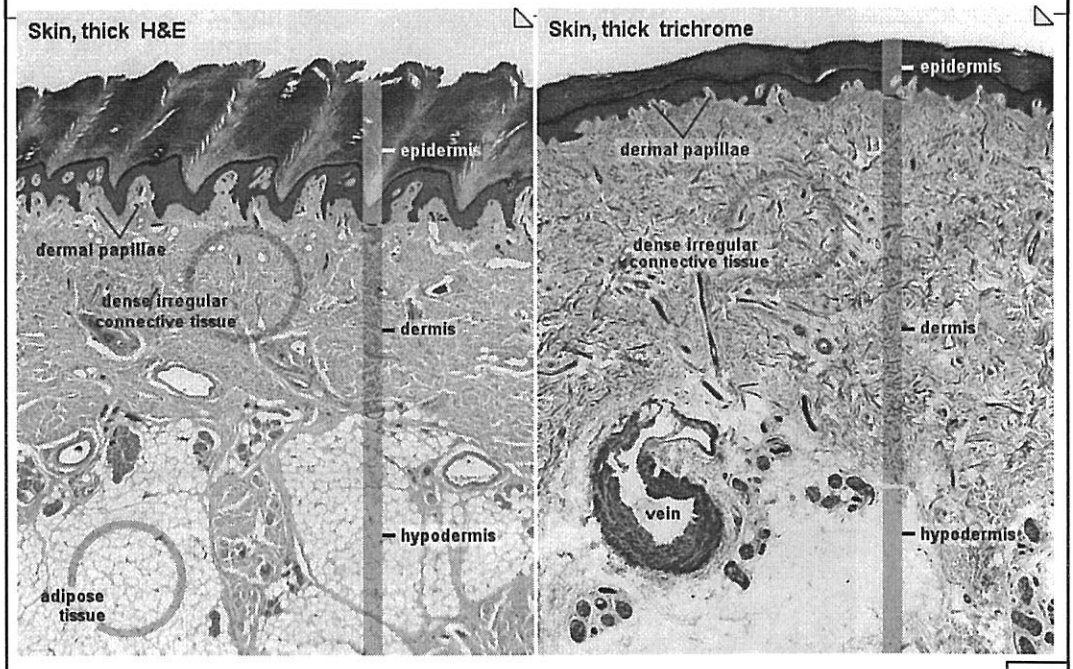

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Skin - Hypodermis (subcutis)

- The hypodermis is not part of the skin but is the superficial fascia of gross anatomical dissection that covers the entire body, immediately deep to the skin.
- The hypodermis, a loose connective tissue containing varying amounts of fat, underlies the skin.
- The hypodermis provides
  - nutritional storage,
  - cushioning, and
  - insulation.
- Individuals who are overnourished or who live in cold climates possess a large amount of fat deposited in the superficial fascia (hypodermis), named panniculus adiposus.

- In certain regions of the body, the skin displays different textures and thicknesses.
- For example,
  - skin of the eyelid is soft, fine, and thin and has fine hairs,
  - skin of the eyebrow is thicker and manifests coarse hair,
  - skin of the forehead produces oily secretions,
  - skin on the chin lacks oily secretions but develops much hair.
  - skin of the palms of the hands and soles of the feet are thick and do not produce hair but contain many sweat glands.

- Finger and toe pad surfaces have well-defined, alternating ridges and grooves that form patterns of loops, curves, arches, and whorls called dermatoglyphs (fingerprints), which develop in the fetus and remain unchanged throughout life.
- Dermatoglyphs are so individualized that they are used for identification purposes in forensic medicine and in criminal investigations.
- Although fingerprints are determined genetically, perhaps by multiple genes,
- Changes in skin colour (e.g., jaundice) or texture may be clues to systemic disorders.
  - Skin disorders range from dermatitis and acne to skin cancer.

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Epidermis

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Epidermis

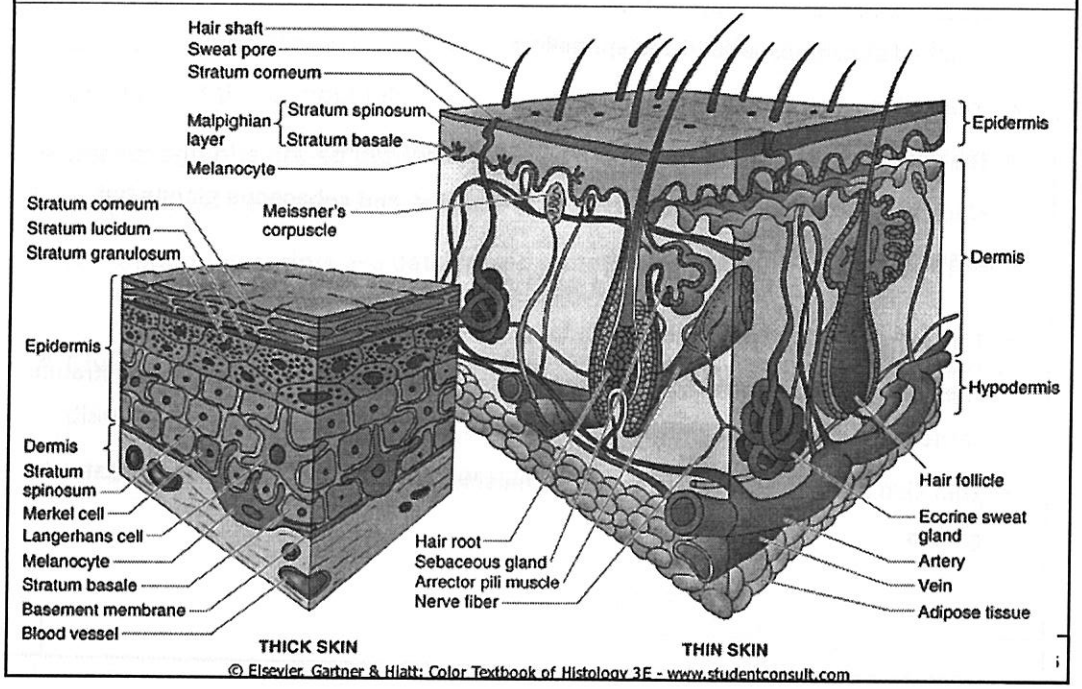
- Epidermis, the surface layer of skin, is derived from ectoderm and is composed of stratified squamous keratinized epithelium.
- Thick skin covers the palms and soles.
- The epidermis of thick skin, which is 400 to 600 um thick.
- Thick skin lacks hair follicles, arrector pili muscles, and sebaceous glands but possess sweat glands.
- Thin skin covers most of the remainder of the body.
- The epidermis of thin skin, which ranges from 75 to 150 um thick, has a thin stratum corneum and lacks a definite stratum lucidum and stratum granulosum.
- Thin skin has hair follicles, arrector pili muscles, sebaceous glands, and sweat glands.

Stratified Squamous Keratinized Epithelium of Epidermis

- Stratified squamous keratinized epithelium of skin is composed of four populations of cells:
  - Keratinocytes : largest population = epithelial cells
  - Langerhans cells
  - Melanocytes
  - Merkel cells

Skin consists of two layers:

1. an outer = epidermis and
2. a deeper connective tissue layer = dermis

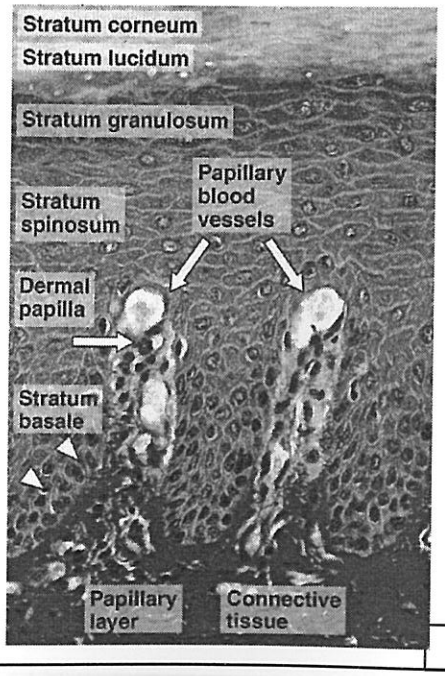


Cytomorphosis of Epidermis

- Five morphologically distinct zones of the epidermis :

  Stratified Squamous Keratinized Epithelium

  - 1. stratum basale (germinativum),
  - 2. stratum spinosum,
  - 3. stratum granulosum,
  - 4. stratum lucidum, and
  - 5. stratum corneum.



Keratinocytes

- Because keratinocytes are continually being sloughed from the surface of the epidermis.
- Keratinocytes undergo mitosis at night in the basal layers, the cells above continue to be pushed toward the surface, the cells differentiate and begin to accumulate keratin filaments in their cytoplasm. Eventually, as they near the surface, the cells die and are sloughed off, a process that takes 20 to 30 days.
- The structural protein produced by the keratinocytes is keratin, which forms 10-nm filaments.
- Growth and development of keratinocytes are influenced by epidermal growth factor (EGF) and interleukin (IL-1α).

Strata and Histological Features of Epidermis

Layer	Histological Features
Epidermis	Derived from ectoderm; composed of stratified squamous eratinized epithelium (keratinocytes)
Stratum corneum	Numerous layers of dead flattened keratinized cells, keratinocytes, without nuclei and organelles (squames, or horny cells) that will be sloughed off
Stratum lucidum*	Lightly stained thin layer of keratinocytes without nuclei and organelles; cells contain densely packed keratin filaments and eleidin
Stratum granulosum*	A layer three to five cell layers thick; these keratinocytes still retain nuclei; cells contain large, coarse keratohyalin granules as well as membrane-coating granules
Stratum pinosum	Thickest layer of epidermis, whose keratinocytes, known as prickle cells, interdigitate with one another by forming intercellular bridges and a large number of desmosomes; prickle cells have numerous tonofilaments and membrane-coating granules and are mitotically active; this layer also houses Langerhans cells
Stratum basale (germinativum)	This single layer of cuboidal to low columnar, mitotically active cells is separated from the papillary layer of the dermis by a well-developed basement membrane; Merkel cells and melanocytes are also present in this layer

1. Stratum Basale (Stratum Germinativum)

- The stratum basale consists of a single layer of mitotically active, cuboidal to low columnar cells containing basophilic cytoplasm and a large nucleus.
- The basale cells synthesize keratins.
- Many desmosomes are located on the lateral cell membrane attaching stratum basale cells to each other and to cells of the stratum spinosum.
- Basally located hemidesmosomes attach the cells to the basal lamina.
- The stratum basale is the germinal layer that undergoes mitosis.
- When new cells are formed, the previous layer of cells is pushed surfaceward to join the next layer of the epidermis, the stratum spinosum.

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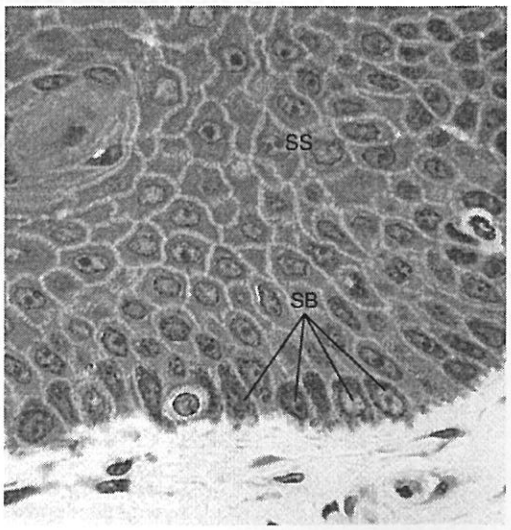
Stratum Basale



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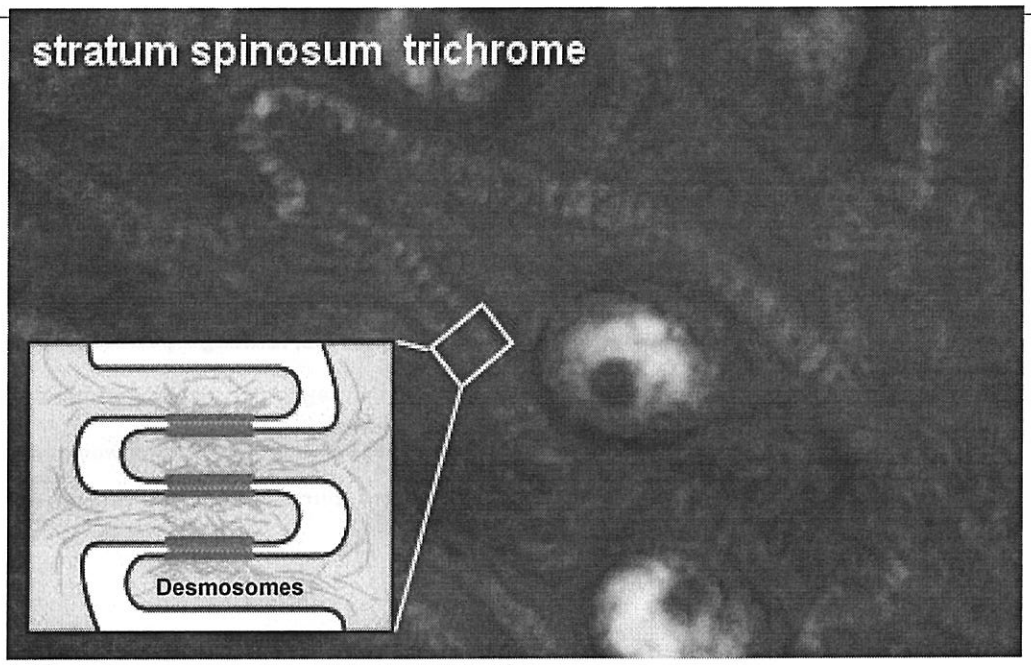
2. Stratum Spinosum

- The thickest layer of the epidermis, composed of polyhedral to flattened cells. The basally located keratinocytes in the stratum spinosum also are mitotically active.
- Stratum basale and stratum spinosum together, referred to as the malpighian layer, are responsible for the turnover of epidermal keratinocytes.
- Cells of the stratum spinosum also produce and deposit the protein involucrin.
- Cells of the stratum spinosum also form the membrane-coating granules, which later release their lipid-rich contents into the intercellular spaces, forming a permeability barrier.

Stratum Spinosum

- the cells in the stratum spinosum are richer in bundles of intermediate filaments (tonofilaments).
- In the stratum spinosum cells, the adjacent cells attach to each other by desmosomes.
- As keratinocytes move toward the surface through the stratum spinosum, they continue to produce tonofilaments, which become grouped in bundles called tonofibrils, causing the cytoplasm to become eosinophilic.
- The flattened vesicles house lipid substance arranged in a closely packed, lamellar configuration.

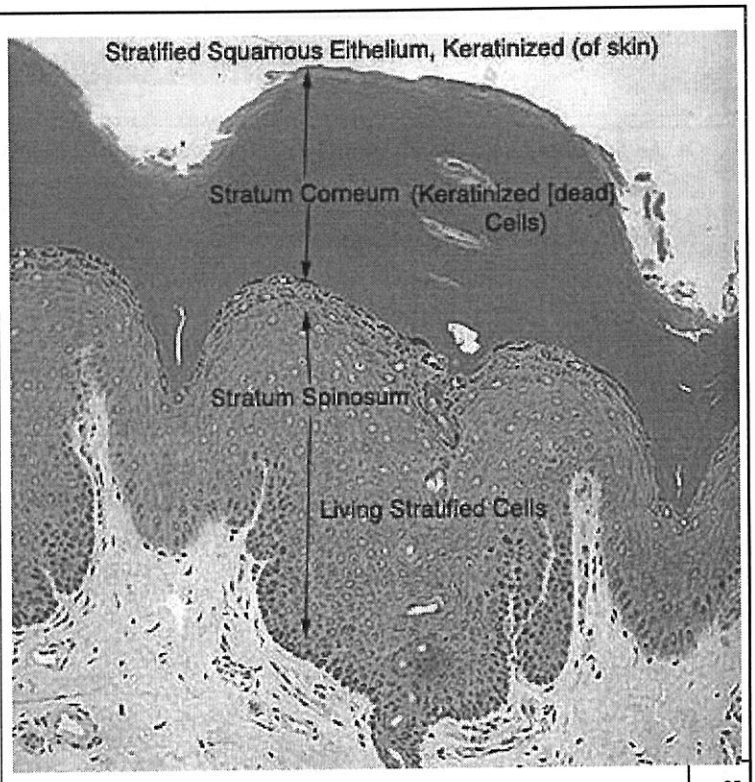
Stratum Spinosum



3. Stratum Granulosum

- **The stratum granulosum, consisting of 3-5 layers of flattened keratinocytes, the cells still possess nuclei.**
- **The cytoplasm of these keratinocytes contains large, irregularly shaped, coarse, basophilic keratohyalin granules, which are not membrane-bound.**
- **Bundles of keratin filaments pass through these granules.**
- **The cells in this layer produce filaggrin, a protein thought to help assemble keratin filaments into still coarser bundles.**

Stratum Granulosum



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Stratum Granulosum

- Once keratinocytes reach this stratum, the keratin-synthesizing machinery shuts down and they also become permeable to calcium ions, which assist in cross-linking involucrin with other proteins, thereby forming a tough layer beneath the plasmalemma.
- The cells of the stratum granulosum also contain membrane-coating granules.
- The contents of these granules are released by exocytosis into the extracellular space, forming sheets of lipid-rich substance that acts as a waterproof barrier, one of the functions of skin.
- This impermeable layer prevents cells lying superficial to this region from being bathed in the nutrient-filled aqueous extracellular fluid, thus hastening their death.

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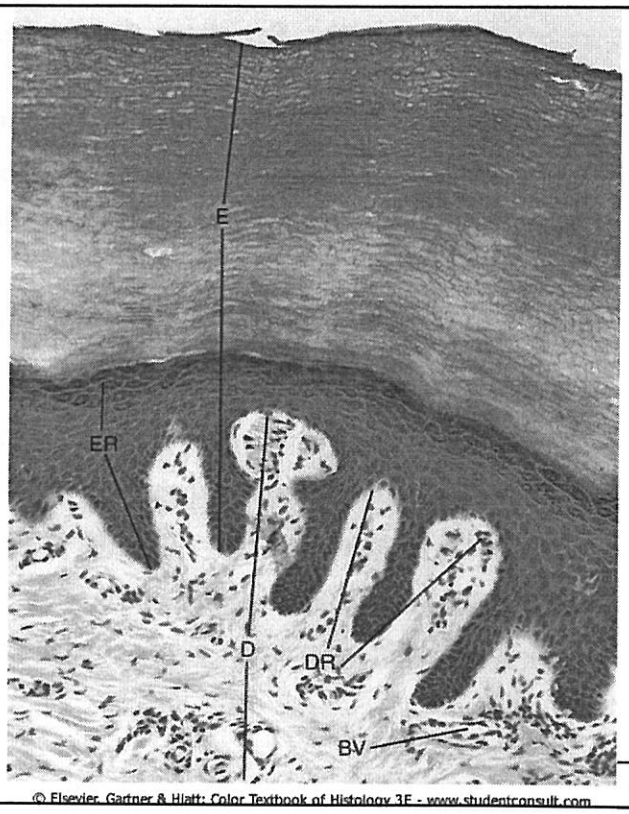
4. Stratum Lucidum

- As keratinocytes move through the stratum granulosum into the stratum lucidum, enzymes released from lysosomes digest the organelles and the nucleus.
- The clear, homogeneous, lightly staining, thin layer of cells immediately superficial to the stratum granulosum is the stratum lucidum.
- This layer is present only in thick skin (i.e., palms of the hands and soles of the feet).
- The flattened cells lack organelles and nuclei, they contain densely packed keratin filaments oriented parallel to the skin surface and eleidin, a transformation product of keratohyalin.
- The cytoplasmic aspect of the plasma membrane of these cells has a thickened appearance because of the deposition of a nonkeratin protein, known as involucrin, whose function is not known.

Stratum lucidum



5. Stratum Corneum

- When the cells finally enter the stratum corneum, they are nonliving, organelle-free, tough shells filled with bundles of keratin filaments.
- The most superficial layer of the stratum corneum, is composed of numerous layers of flattened *as squames*, keratinized cells with a thickened plasmalemma.
- The cells farther away from the skin surface display desmosomes.
- The cells near the surface of the skin, called squamas, or horny cells, lose their desmosomes and become desquamated (sloughed off).

Stratum Corneum

- 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.

Nonkeratinocytes in the Epidermis

Langerhans Cells

- ***Langerhans cells are antigen-presenting cells located among the cells of the stratum spinosum.***
- **Langerhans cells, sometimes called dendritic cells because of their numerous long processes, are located primarily in the stratum spinosum.**
- **These cells are scattered throughout the epidermis and also may be found in the dermis as well as in the stratified squamous epithelia of the oral cavity, esophagus, and vagina.**
- **Langerhans cells are originate from precursors in the bone marrow and are a part of the mononuclear phagocyte system, function in the immune response by presenting epitopes of processed foreign antigens to T lymphocytes.**

Merkel Cells

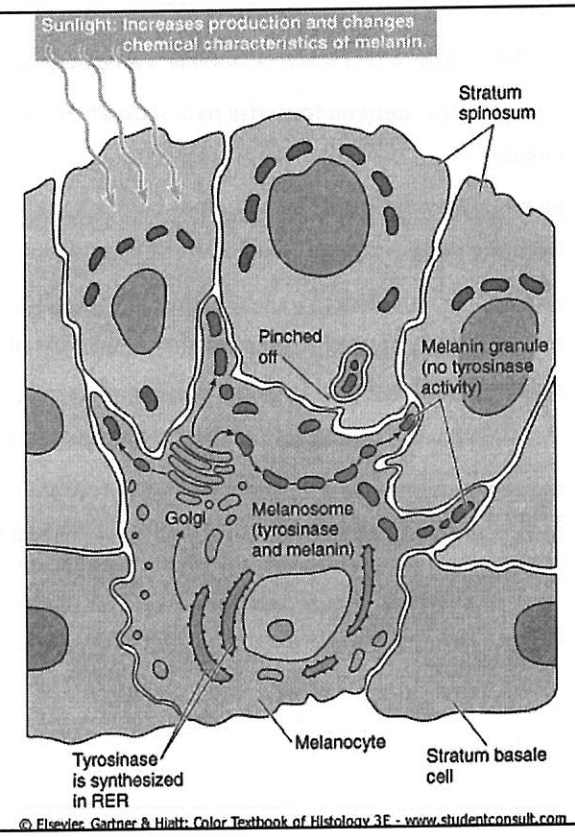
- **Derived from the neural crest, which are interspersed among the keratinocytes of the stratum basale of the epidermis, are especially abundant in the fingertips and oral mucosa and at the base of hair follicles.**
- **Myelinated sensory nerves traverse the basal lamina to approximate the Merkel cells, thus forming Merkel cell-neurite complexes.**
- **These complexes may function as mechanoreceptors.**
- **These cells exhibit a synaptophysin-like immunoreactivity, indicating that Merkel cells may release neurocrine-like substances, suggesting that the cells display diffuse neuroendocrine system-related activity.**

Melanocytes

- Melanocytes, derived from the neural crest, are located among the cells of the stratum basale,
- Melanocytes are round to columnar cells whose long, undulating processes extend from the superficial surfaces of the cells and penetrate the intercellular spaces of the stratum spinosum.
- Melanocyte is packaged by oval granules known as melanosomes, where tyrosinase converts it into melanin.
- The enzyme tyrosinase is activated by ultraviolet light.
- the melanosomes are transported to the supranuclear region so that the melanosomes form a protective barrier between the nucleus and the impinging ultraviolet rays from the sun.

- Melanosomes leave the cell body of the melanocytes and travel to the tips of their long processes.
- the tips of the melanocyte processes penetrate the cytoplasm of the stratum spinosum cells and become pinched off via a special secretory process called cytocrine secretion.
- A particular melanocyte serves a number of keratinocytes with which it is associated, constituting an epidermal melanin unit.
- Eventually, the melanin pigment is attacked and degraded by lysosomes of the keratinocyte.

Melanocyte



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Dermis (Corium)

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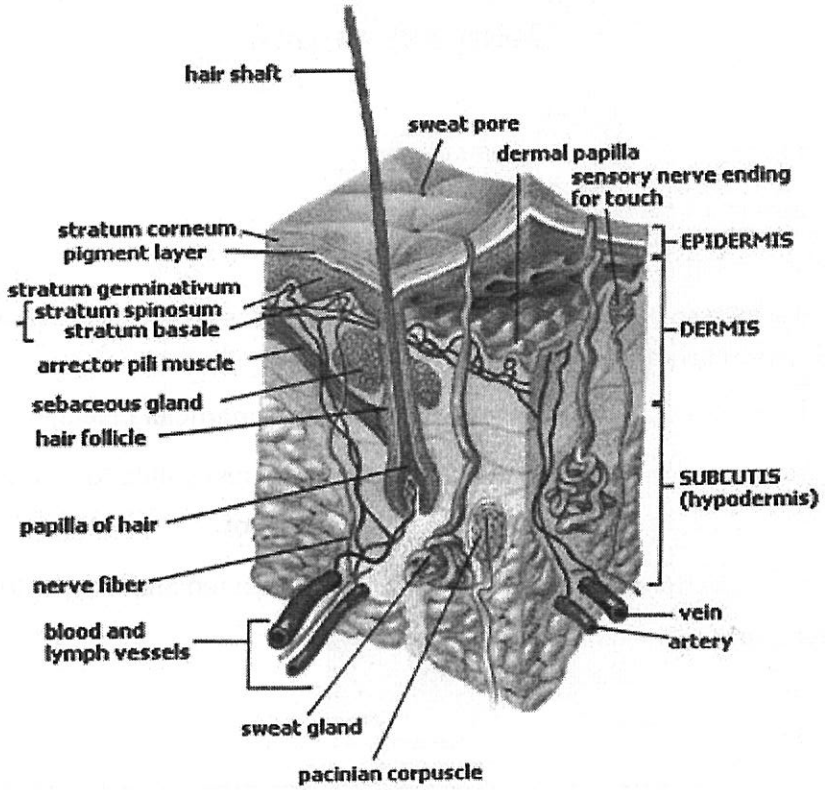
Dermis (Corium)

- *The dermis is derived from mesoderm.*
- The dermis comprises
  - papillary layer, loose and
  - reticular layer, deeper, denser irregular connective tissue containing networks of collagen fibers and elastic fibers
- The dermis binds epidermis and hypodermis (superficial fascia).
- The dermis ranges in thickness from 0.6 mm in the eyelids to 3 mm or so on the palm of the hand and the sole of the foot.
- Normally, the dermis is thicker in men than in women and on the dorsal rather than on the ventral surfaces of the body.

Strata and Histological Features of Dermis

Layer	Histological Features
Dermis	Derived from mesoderm; composed mostly of type I collagen and elastic fibers, the dermis is subdivided into two regions: the papillary layer and the reticular layer, a dense, irregular collagenous connective tissue
Papillary layer	Interdigitates with epidermis, forming the dermal papilla component of the rete apparatus; type III collagen and elastic fibers in loose arrangement and anchoring fibrils (type VII collagen); abundant capillary beds, connective tissue cells, and mechanoreceptors are located in this layer; occasionally, melanocytes are also present in the papillary layer
Reticular layer	Deepest layer of skin; type I collagen, thick elastic fibers, and connective tissue cells; contains sweat glands and their ducts, hair follicles and arrector pili muscles, and sebaceous glands as well as mechanoreceptors (such as pacinian corpuscles)



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Papillary Layer of the Dermis

- The superficial papillary layer of the dermis is uneven where it interdigitates with the epidermis, forming the dermal ridges (papillae)
- It is composed of a loose connective tissue whose thin, reticular fibers and elastic fibers are arranged in loose networks.
- Anchoring fibrils, composed of collagen, extend from the basal lamina into the papillary layer and bind the epidermis to the dermis.
- The papillary layer contains fibroblasts, macrophages, plasma cells, mast cells, and other cells common to connective tissue.
- The papillary layer also possesses many capillary loops, which extend to the epidermis-dermis interface.

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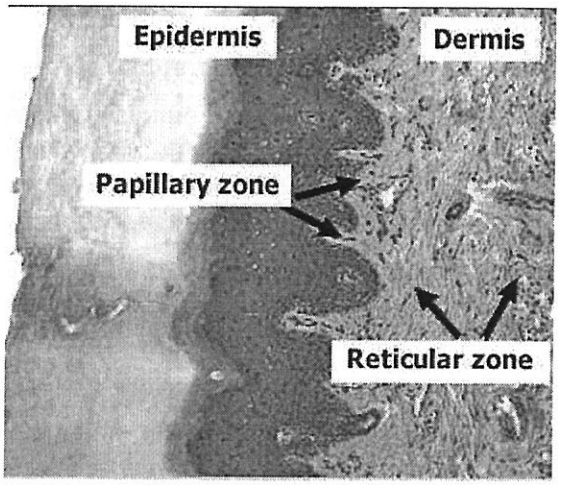
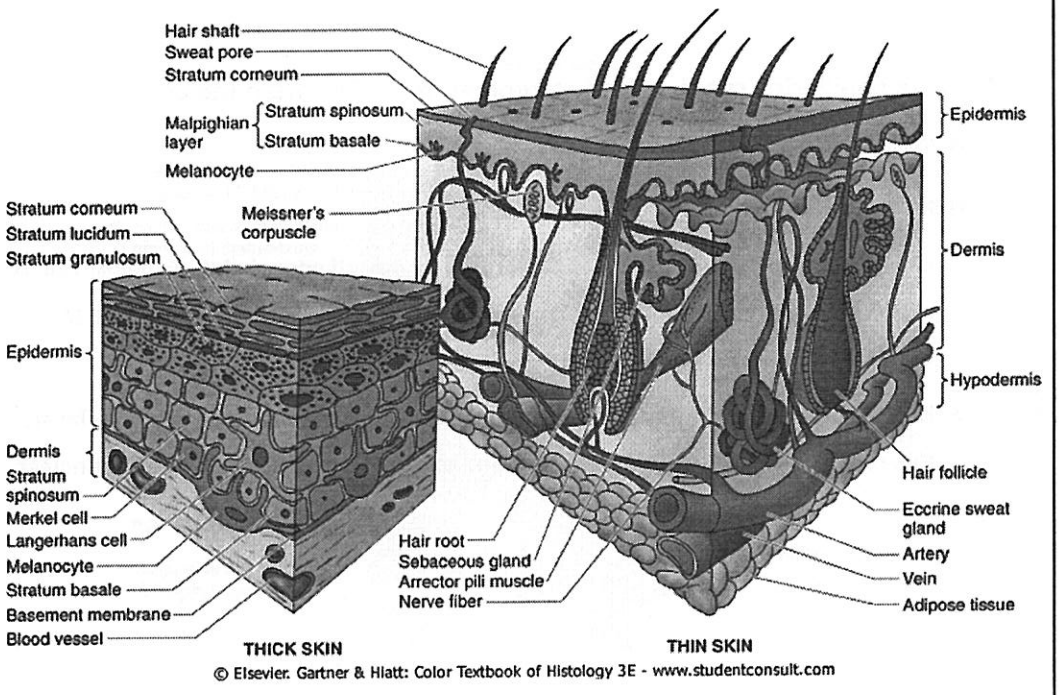
Papillary Layer of the Dermis

- These capillaries regulate body temperature and nourish the cells of the avascular epidermis.
- In some dermal papillae, there are
  - Meissner corpuscles, mechanoreceptors, pear-shaped encapsulated specialized to respond to slight deformations of the epidermis and are especially sensitive to tactile stimulation (e.g., lips, external genitalia, and nipples).
  - Krause end bulb, encapsulated mechanoreceptor, is present in the papillary layer, this receptor was once thought to respond to cold, its function is currently unclear.

Dermis Section





Reticular Layer of the Dermis

- ***The reticular layer of the dermis also contains epidermally derived structures, including sweat glands, hair follicles, and sebaceous glands.***
- **The reticular layer is composed of dense, irregular collagenous connective tissue, which are closely packed into large bundles lying mostly parallel to the skin surface.**
- **Networks of thick elastic fibers are intermingled with the collagen fibers, appearing especially abundant near sebaceous and sweat glands.**
- **Cells are more sparse in this layer than in the papillary layer.**
- **They include fibroblasts, mast cells, lymphocytes, macrophages, and, frequently, fat cells in the deeper aspects of the reticular layer.**

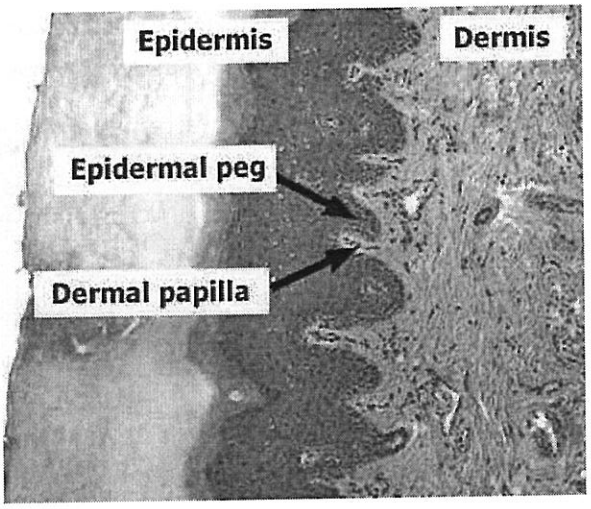
Reticular Layer of the Dermis

- Groups of smooth muscle cells are located in the deeper regions of the reticular layer at particular sites such as the skin of the penis and scrotum and the areola around the nipples;
  - contractions of these muscle groups wrinkle the skin in these regions.
- Other smooth muscle fibers, called arrector pili muscles, are inserted into the hair follicles;
  - contractions of these muscles erect the hairs when the body is cold or suddenly exposed to a cold environment, giving the skin "goose bumps."
- At least two types of encapsulated mechanoreceptors are located in the deeper portions of the dermis:
  - (1) pacinian corpuscles, which respond to pressure and vibrations, and
  - (2) Ruffini corpuscles, which respond to tensile forces.

Epidermis-Dermis Interface

- *The interdigitation of the epidermal ridges with the dermal ridges is known as the rete apparatus.*
- The interdigitations of the epidermal and dermal layers are translated through the epidermis and are apparent on the surface of the skin, especially of the palms and soles, where they are represented by whorls, arches, and loops of dermatoglyphs or fingerprints.
- The papillary layer presents parallel primary dermal ridges on its surface separated by primary grooves, which house projections of the epidermis
- In the center of each primary dermal ridge is a secondary groove, which receives a downgrowth of the epidermis known as an interpapillary peg.
- Along this and other adjacent ridges are rows of round-topped dermal papillae that project into concavities in the epidermis, thus firmly interlocking the epidermis and dermis at the interface.

Interpapillary Pegs



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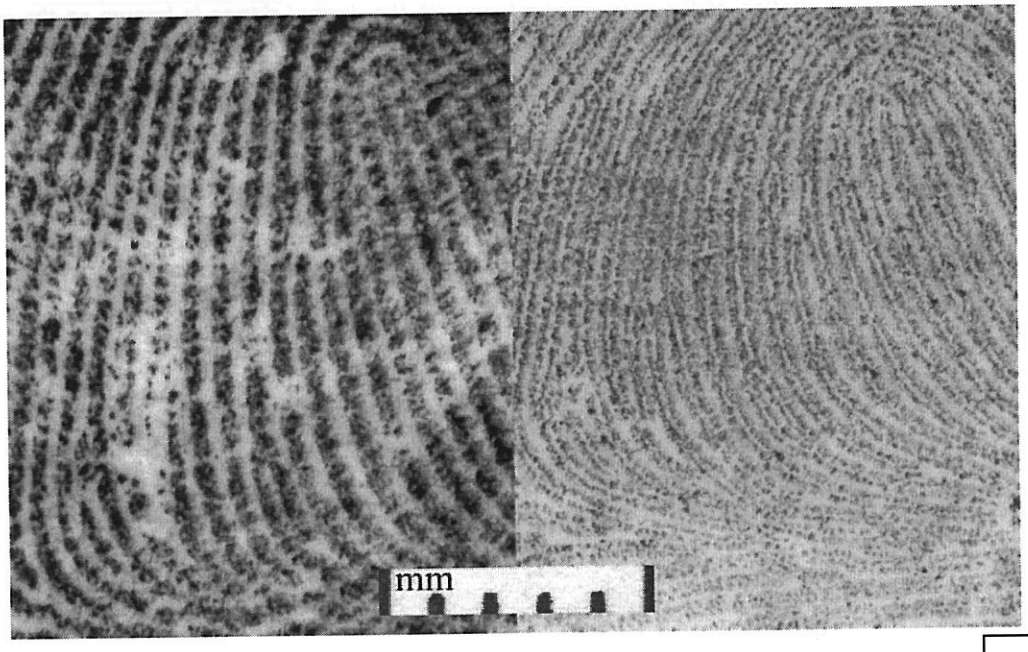
Dermatoglyphs or Fingerprints in Rete Apparatus



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Glands of the Skin

eccrine (merocrine sweat) glands,

apocrine sweat glands,

sebaceous glands,

mammary gland

Eccrine sweat glands

- ***Eccrine sweat glands are simple coiled tubular glands located deep in the dermis, open on the surface of the skin at a sweat pore.***
- **They release their secretory product, sweat, via the merocrine method of secretion (intact cells).**
- **The secretory portion of the gland is composed of dark cells and clear cells,**
  - **Dark cells line the lumen of the secretory unit and secrete a mucus-rich substance containing ions, urea, lactic acid, and some drugs**
  - **Clear cells do not possess secretory granules; they release a watery secretion.**

Eccrine sweat glands

- The secretion is similar to blood plasma in regard to electrolyte balance, including potassium and sodium chloride as well as ammonia and urea.

- The secretion is hypotonic to the plasma.
- It is the evaporation of this secretion on the surface of the skin that aids in thermoregulation.
- However, most of the potassium, sodium, and chloride ions are reabsorbed by cells of the duct as the secretion travels through its lumen.
- Myoepithelial cells surrounding the secretory portion of the gland contain actin and myosin, imparting a contractile ability to these cells.

Eccrine sweat glands

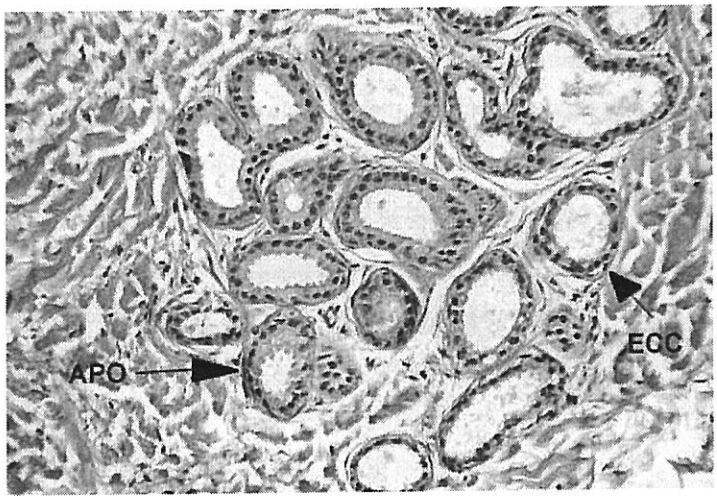
Apocrine sweat glands

- Apocrine sweat glands are found only in the axilla, areola of the nipple, and anal region and may represent vestigial scent glands.
- Apocrine sweat glands are arises from the epithelium of the hair follicles, much larger than eccrine sweat glands, up to 3 mm in diameter.
- Modified apocrine sweat glands constitute the ceruminous (wax) glands of the external auditory canal and the glands of Moll in the eyelids
- The viscous secretory product of apocrine glands is odorless upon secretion, but when bacteria metabolized 3-methyl-1,2-hexanoic acid - a volatile acid similar to pheromone signals, it presents a distinctive odor.

Apocrine sweat glands

- Secretion by apocrine glands is under the influence of hormones and does not begin until puberty.
- Apocrine sweat glands in women undergo cyclical changes that seem to be related to the menstrual cycle-that is, the secretory cells and lumina enlarge before the premenstrual period and diminish during menstruation.
- Apocrine sweat glands release their secretory product via the merocrine mode of secretion.
- Myoepithelial cells surround the secretory portion of the apocrine sweat glands and assist in expressing the secretory product into the duct of the gland.

Apocrine sweat glands



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Sebaceous Glands

- Sebaceous glands secrete an oily substance known as sebum, which maintains the suppleness of the skin.
- Sebaceous glands are found throughout the body, except for the palms of the hands, soles of the feet, and sides of the feet inferior to the hairline.
- Sebaceous glands are embedded in the dermis and hypodermis.
- These glands are most abundant on the face, scalp, and the forehead.
- The secretory product of the sebaceous glands, sebum, is a wax-like, oily mixture of cholesterol, triglycerides, and secretory cellular debris.
- Sebum is believed to facilitate the maintenance of proper skin texture and hair flexibility.

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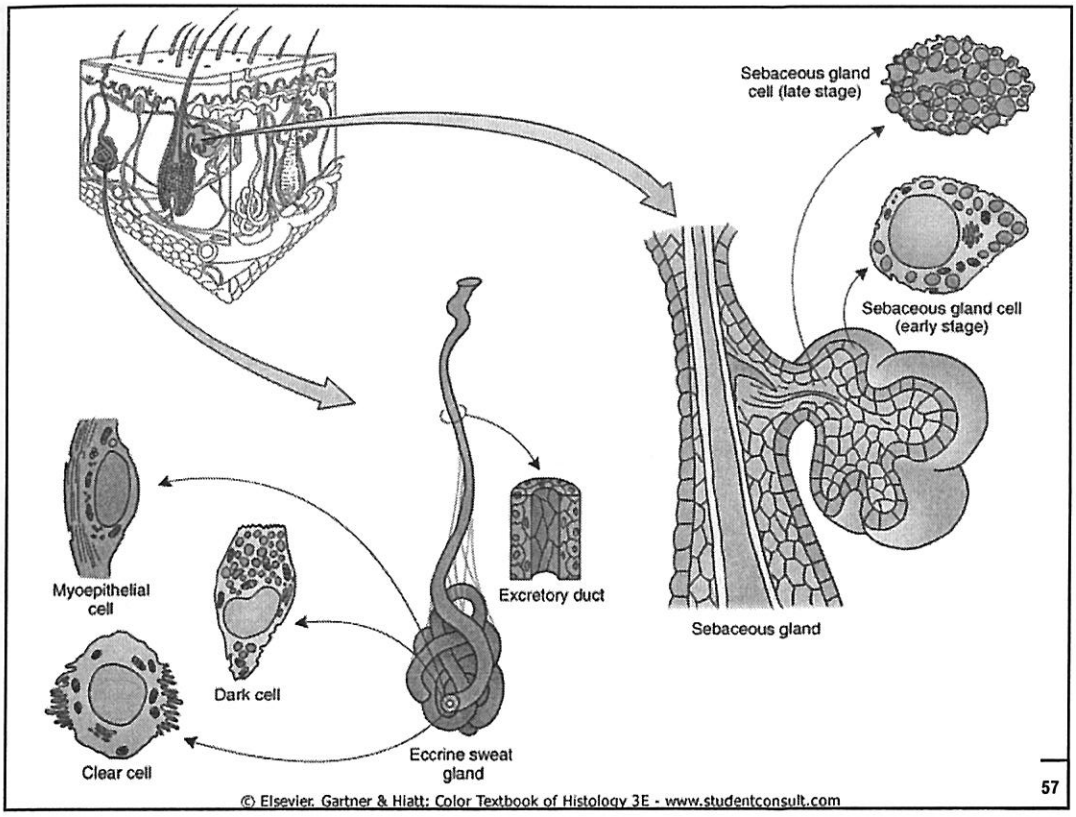

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- The ducts of the sebaceous glands open into the upper third of the follicular canal, where they discharge their secretory product to coat the hair shaft and, eventually, the skin surface
- Sebaceous glands are lobular with clusters of acini opening into single short ducts.
- Each acinus is composed of peripherally located small basal cells (resting on the basal lamina)
- The central region of the acinus is filled with cells in different stages of degeneration.
- Lipid synthesis continues for a short time, followed by necrosis of the cells and the ultimate release of lipid and cellular debris, which form the secretory product (holocrine secretion – entire cell broken).

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Hair

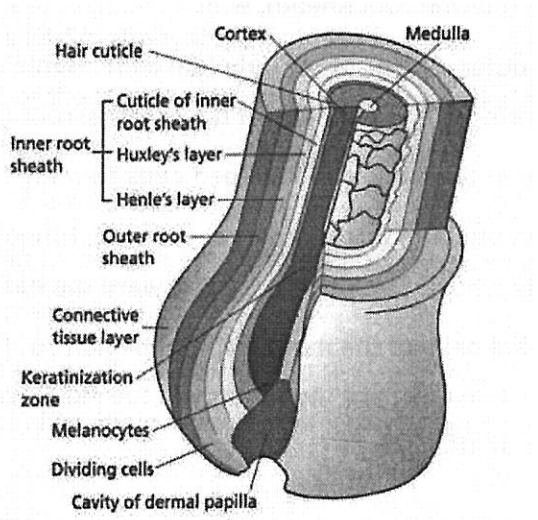
Hair

- Hairs are filamentous, keratinized structures that project from the epidermal surface of the skin
- Hair grows over most of the body except on the vermilion zone of the lips, palms and sides of the palms, soles and sides of the feet, dorsum of the distal phalanges of the fingers and toes, glans penis, glans clitoris, labia minora, and vestibular aspect of the labia majora.
- Two types of hairs are present on the human body.
  - Hairs that are soft, fine, short, and pale (e.g., those covering the eyelids) are called vellus hairs, in primates.
  - Hairs that are hard, large, coarse, long, and dark (e.g., those of the scalp and eyebrows) are called terminal hairs, in humans.
  - Additionally, very fine hair, called lanugo, is present on the fetus.

- Hair growth is optimal from about 16 to 46 years of age; after age 50, hair growth begins to diminish.
- During pregnancy, hair growth is normal; after parturition, the cycle of hair growth subsides and hair loss is temporarily increased.

- Hair follicles, the organs from which hairs develop, arise from invaginations of the epidermis that invade the dermis, hypodermis, or both.
- Hair follicles are surrounded by dense accumulations of fibrous connective tissue belonging to the dermis
- The hair root, is indented, and the concavity conforms to the shape of the dermal papilla occupying it.
- The hair root and the dermal papilla together are known as the hair bulb.

Hair Bulb



The structure of the hair bulb

- The dermal papilla contains a rich supply of capillaries that provide nutrients and oxygen for the cells of the hair follicle.
- The dermal papilla also acts as an inductive force controlling the physiological activities of the hair follicle.
- Proliferation of these matrix cells accounts for the growth of hair; thus, they are homologous to the stratum basale of the epidermis.
- The outer layers of follicular epithelium form the external root sheath, which is composed of a single layer of cells at the hair bulb and several layers of cells near the surface of the skin
- The internal root sheath ends where the duct of the sebaceous gland attaches to the hair follicle

- The internal root sheath, which consists of three components:

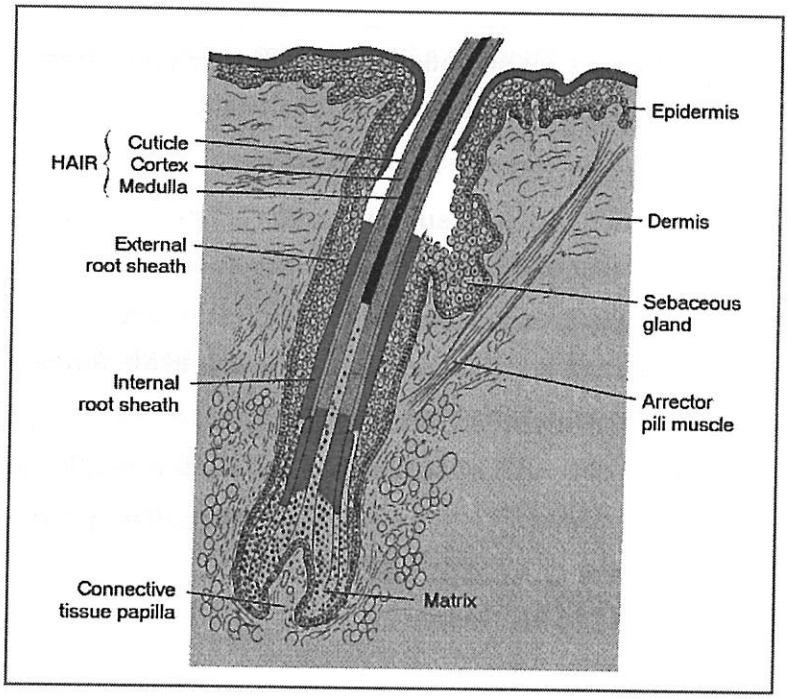
(1) an outer single row of cuboidal cells, Henle's layer, which contacts the innermost layer of cells of the external root sheath;

(2) one or two layers of flattened cells forming Huxley's layer; and

(3) the cuticle of the internal root sheath, formed by overlapping scale-like cells whose free ends project toward the base of the hair follicle.

- As the cells of the matrix within the hair root proliferate and differentiate, they move toward the surface of the skin, eventually developing into the hair shaft.

Hair follicle



65

- As the cells of the cortex are displaced surfaceward, they synthesize abundant keratin filaments and trichohyalin granules
- Scattered among the cells of the matrix nearest to the dermal papilla are large melanocytes, with long dendritic processes that transfer melanosomes to the cells of the cortex.
- The melanosomes remain in these cells, imparting to the hair a color based on the amount of melanin present.
- With age, the melanocytes gradually lose their ability to produce tyrosinase, which is essential for the production of melanin, and the hair becomes gray.

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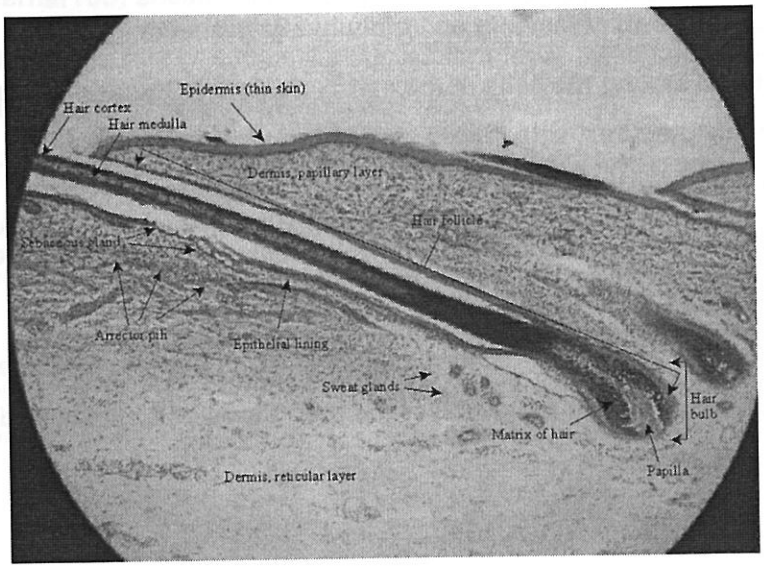
Arrector pili muscles

- Arrector pili muscles are smooth muscle cells extending from midshaft of the hair follicle to the papillary layer of the dermis.
- Attached to the connective tissue sheath surrounding the hair follicles and to the papillary layer of the dermis.
- Contractions of these muscles depress the skin over their attachment and elevate the hair shaft and the skin around the hair shaft, forming tiny "goose bumps" on the surface of the skin.
- These are easily observed when a person is chilled or suddenly frightened.



Hair grows

- Hair grows at an average rate of about 1 cm/month, but hair growth is not continuous.
- The hair growth cycle consists of three successive phases:
  - (1) the growth period, the anagen phase;
  - (2) a brief period of involution, the catagen phase; and
  - (3) the final phase of rest, the telogen phase, in which the mature, aged hair is shed (falls out or is pulled out).
- Hairs shed in this fashion are called club hairs because they retain their club-shaped root. Soon afterward, a new hair is formed by the hair follicle and the hair growth cycle begins again.

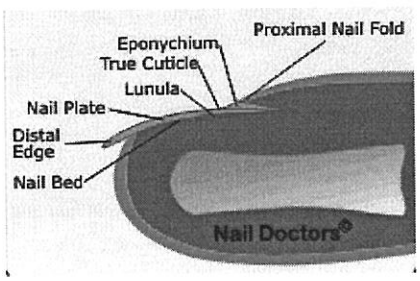
Hairs and Genders

- Hair follicles in certain regions of the body respond to male sex hormones.
- For this reason, men begin to develop more dark-pigmented terminal hairs about the chin, cheeks, and upper lip at puberty.
- Women possess the same number of hair follicles in these regions, these hairs remain the fine, pale, vellus type.
- In both sexes at puberty, however, heavily pigmented, coarse terminal hairs begin to grow in the axillary and pubic regions.

Nails

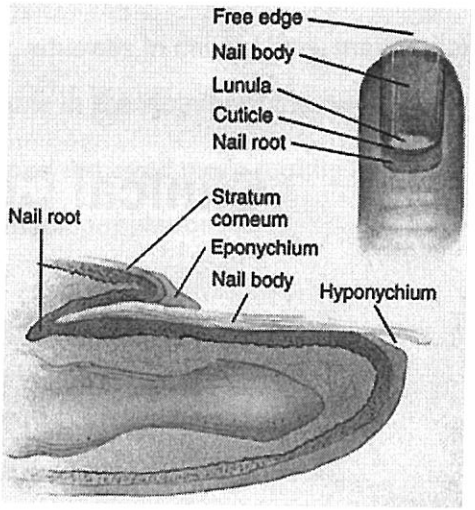
Nail

- Nails represent keratinized epithelial cells arranged in plates of hard keratin.
- Nails, located on the distal phalanx of each finger and toe, compose of
  - Nail plates of heavily compacted, highly keratinized epithelial cells
  - Nail bed lying on the epidermis
- The nails develop from cells of the nail matrix in the nail root
- The nail matrix, a region of the nail root, is located beneath the proximal nail fold.



- The stratum corneum of the proximal nail fold forms the eponychium (cuticle), which extends from the proximal end up on the nail for about 0.5 to 1 mm.
- Laterally, the skin turns under as lateral nail folds, forming the lateral nail grooves; the epidermis continues beneath the nail plate as the nail bed, and the nail plate occupies the position (and function) of the stratum corneum.
- The white crescent observed at the proximal end of the nail is called the lunula.
- The distal end of the nail plate is not attached to the nail bed, which becomes continuous with the skin of the fingertip (or end of the toe). Near this junction is an accumulation of stratum corneum called the hyponychium.

Nail Structure



- Fingernails grow continuously at the rate of about 0.5 mm/week; toenails grow somewhat more slowly.
- The translucency of the fingernails provides a quick indication of the health of an individual.
- Pinkness indicates a well-oxygenated blood supply.

Clinical Correlations

Clinical Correlations

- Ultraviolet light darkens the melanin and speeds tyrosinase synthesis, thus increasing melanin production. Also, pituitary ACTH influences pigmentation.
- In Addison's disease there is insufficient production of cortisol by the adrenal cortex so excess ACTH is produced, which leads to hyperpigmentation.
- Albinism is the absence of melanin production resulting from a genetic defect in tyrosinase synthesis.

  Melanosomes are present but the melanocytes fail to produce tyrosinase.

- In Blacks, melanosomes are large, numerous, and dispersed throughout the cytoplasm of the keratinocytes, whereas in caucasians, melanosomes are smaller and fewer and congregate in the vicinity of the nucleus.

  Also, melanosomes are degraded and removed more rapidly in the Caucasian population than in the Black population.

- Freckles are hyperpigmented spots located on sun-exposed areas of the skin, especially in fair-skinned individuals who sunburn easily.

  Freckles are usually exhibited by 3 years of age and are the result of increased melanin production and accumulation in the basal area of the epidermis without an increase in melanocytes. They tend to fade in the winter and darken with exposure to ultraviolet light.

- Psoriasis is a disease characterized by patchy lesions caused by greater keratinocyte proliferation in the stratum basale and stratum spinosum and an accelerated cell cycle (turnover is increased as much as seven times), resulting in accumulations of keratinocytes and stratum corneum.

  The lesions are common on the scalp, elbows, and knees, but they may occur almost anywhere on the body. In some cases, the nails may also be involved.

  Psoriasis is an incurable but manageable chronic condition whose symptoms periodically escalate and then diminish with no apparent cause.

- Warts are benign epidermal growths caused by infection of the keratinocytes with papillomaviruses.

  The resulting epidermal hyperplasia thickens the epidermis with scaling.

  Deeper ingrowth of the dermis brings capillaries closer to the surface. Warts are common in children, young adults, and immunosuppressed patients.

- Basal cell carcinoma, the most common human malignancy, arises in the stratum basale cells of the epidermis and usually is caused by exposure to ultraviolet radiation.

  Although basal cell carcinomas do not usually metastasize, they are destructive to local tissue.

  Of the several types of lesions that occur, the most common is the nodular variety, characterized by a papule or nodule with a central depressed "crater" that eventually ulcerates and crusts. These lesions are most common on the face, especially the nose. Surgery is the usual treatment, and up to 90% of patients recover with no additional sequelae.

- Squamous cell carcinoma, the second most common skin cancer, arises in the keratinocytes of the epidermis. It is locally invasive and may metastasize.

  It is characterized by a hyperkeratotic scaly plaque or nodule that often bleeds or ulcerates. It invades deeply, resulting in fixation to the underlying tissues.

  Several factors may cause this disease, including ultraviolet radiation, x-irradiation, soot, chemical carcinogens, and arsenic. The lesions are most common on the head and neck.

  Surgery is the usual treatment of choice.

- Malignant melanoma, a skin cancer, is most prevalent in fair-skinned individuals and is increasing in incidence.

  It is usually associated with excessive exposure to the sun. Malignant melanoma is very invasive because the malignant cells originate from transformed melanocytes; the melanocytes penetrate the dermis and enter lymphatic vessels as well as the bloodstream to gain wide distribution throughout the body.

PowerPoint

เรื่อง

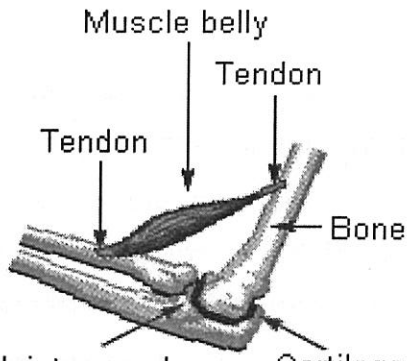
Musculoskeletal System

รองศาสตราจารย์ ดร. กรกช อินทราพิเชฐ

Musculoskeletal System

Musculoskeletal System

- The musculoskeletal system consists of
  - the skeletal system –
    - bones and
    - joints (union of two or more bones) -- and
  - the *skeletal* muscle system (voluntary or striated muscles).



Modified from: DeLisa, Stolov, p. 30

Musculoskeletal System (cont)

- These two systems work together to provide basic functions that are essential to life, including:
  - Protection: protects the brain and internal organs
  - Support: maintains upright posture
  - Blood cell formation: *hematopoiesis*
  - Mineral homeostasis
  - Storage: stores fat and minerals.
  - Leverage: A lever is a simple machine that magnifies speed of movement or force.
    - The levers are mainly the long bones of the body and the axes are the joints where the bones meet.

Musculoskeletal System (cont)

- Each of these contains various combinations of 4 connective tissue building blocks:
  - Fibroblasts - the "mother" cell, producing the other 3 connective tissue components.
  - Collagen - the principal protein manufactured by the fibroblast. Organized into various configurations, these long, thin fibers intertwine to form very strong fibers which do NOT stretch.
  - Elastic fibers - highly elastic fibers, unlike collagen, particularly abundant in the walls of arteries.
  - Proteoglycans - the "ground substance," or "matrix," in which fibroblasts, collagen, and elastic fibers reside.

Muscle Cell Types

Tissues that contract to create movement.

Skeletal muscle

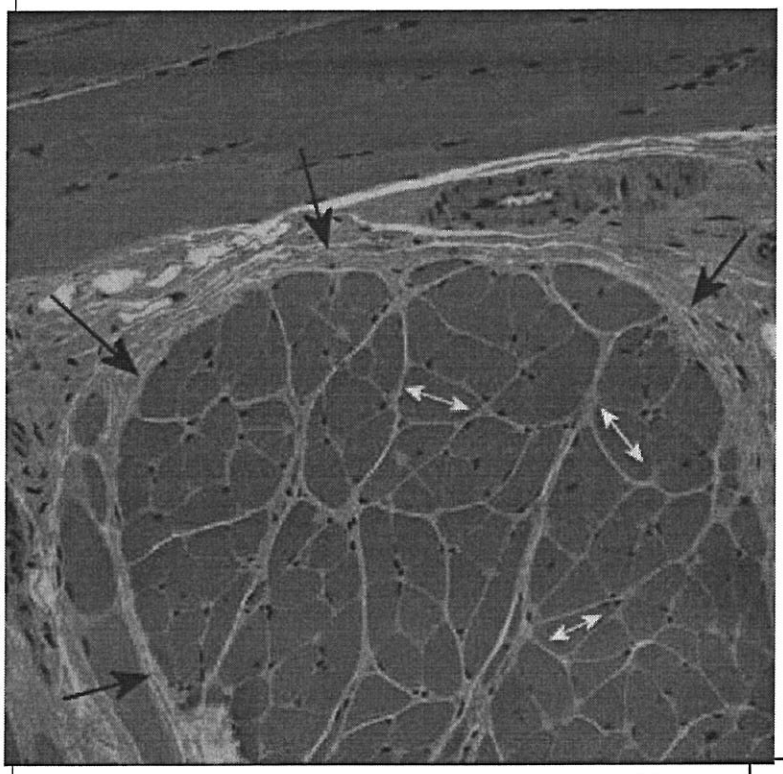
Cardiac muscle

Smooth muscle

Skeletal (voluntary / striated) muscle

- The most abundant tissue in the human body, producing movement.
- Each skeletal-muscle fiber is cylindrical, contains many nuclei, and is crossed by alternating light and dark bands called *striations*.
- Fibers bind together, via connective tissue, into bundles; and these bundles, in turn, bind together to form muscles.
- Thus, skeletal muscles are composite structures composed of many muscle fibers, nerves, blood vessels, and connective tissue.
- Skeletal muscles are controlled by the somatic nervous system (SNS).

Skeletal muscle



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Smooth muscles

- Smooth muscle surrounds many arteries and contracts to adjust blood flow.
- It surrounds the intestines and contracts to move food and feces along the digestive tract.
- Smooth muscle also is controlled by the brain but not voluntarily.
- The triggers for contracting and relaxing smooth muscles are controlled by the body's needs, but they operate without a person's awareness.

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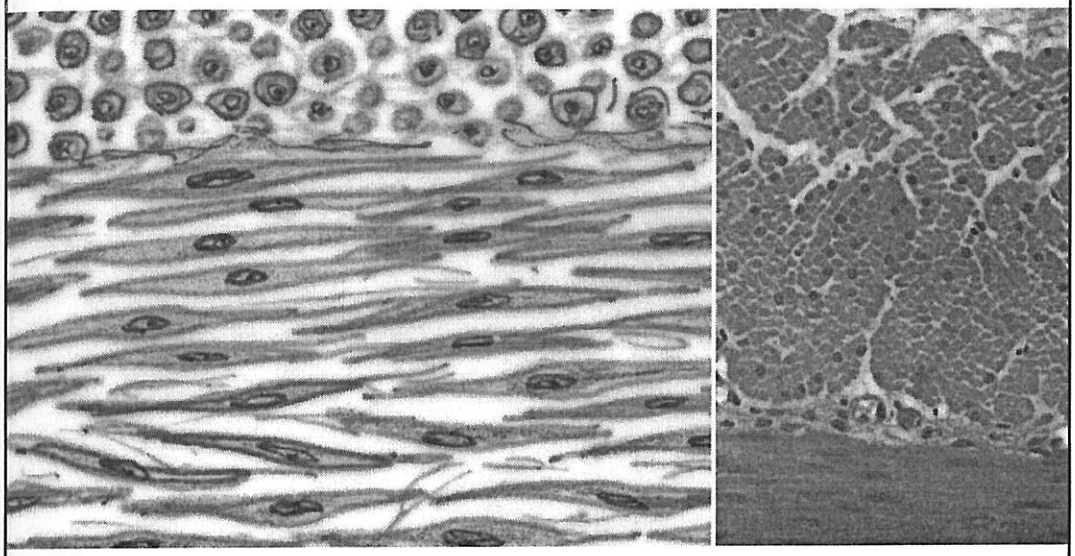
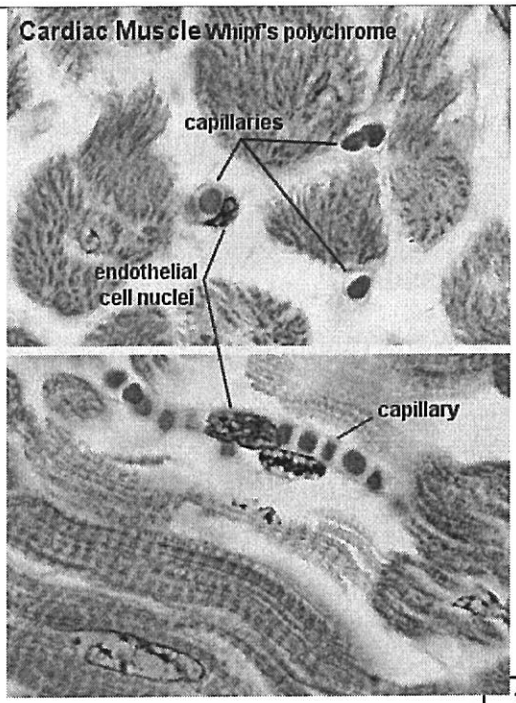
Smooth muscle



Cardiac muscle

- Forms the heart and is not part of the musculoskeletal system.
- Like skeletal muscle, cardiac muscle has a regular pattern of fibers that also appear as stripes under a microscope.
- However, cardiac muscle contracts and relaxes rhythmically without a person's awareness.

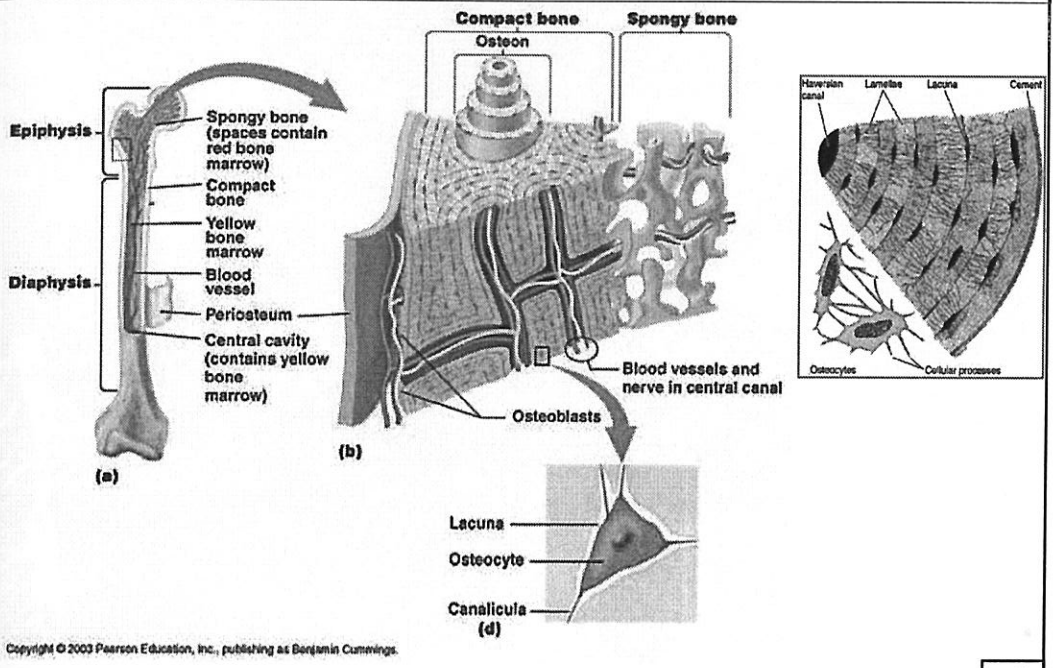


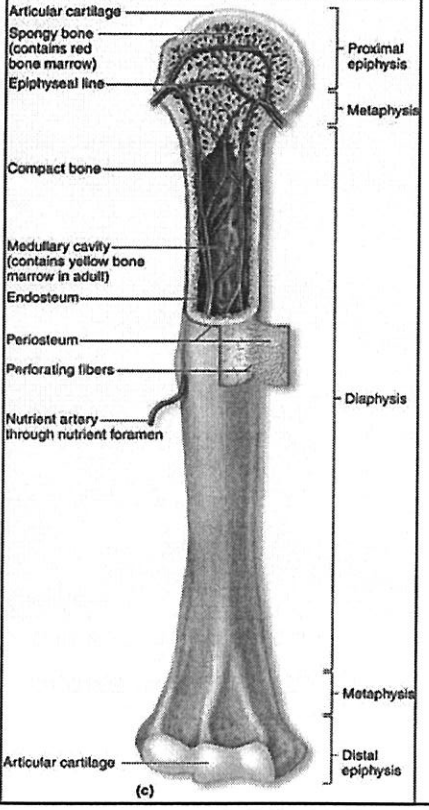
Bones, Cartilage, Tendon, Bursa & Ligament,

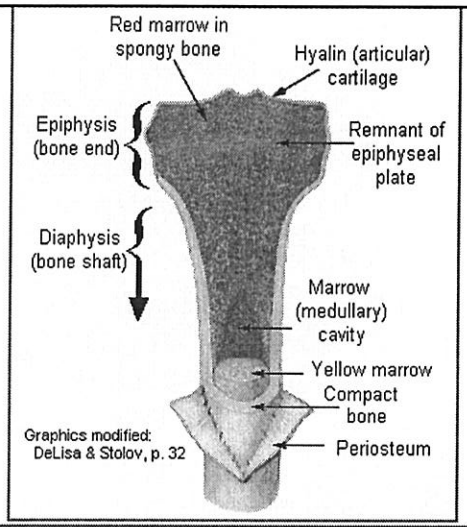
Bone

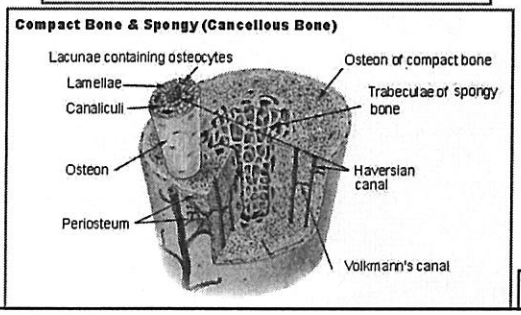
- The human skeleton consists of more than 200 individual bones, all fulfilling different tasks.
- In addition to cartilage tissue, our bodies are supported by bone tissue.
- Bone tissue provides protection for the soft parts underneath it and serves as a point of insertion for the muscles.
  Another important role of bone is its metabolic activity (calcium household, blood formation in red bone marrow).

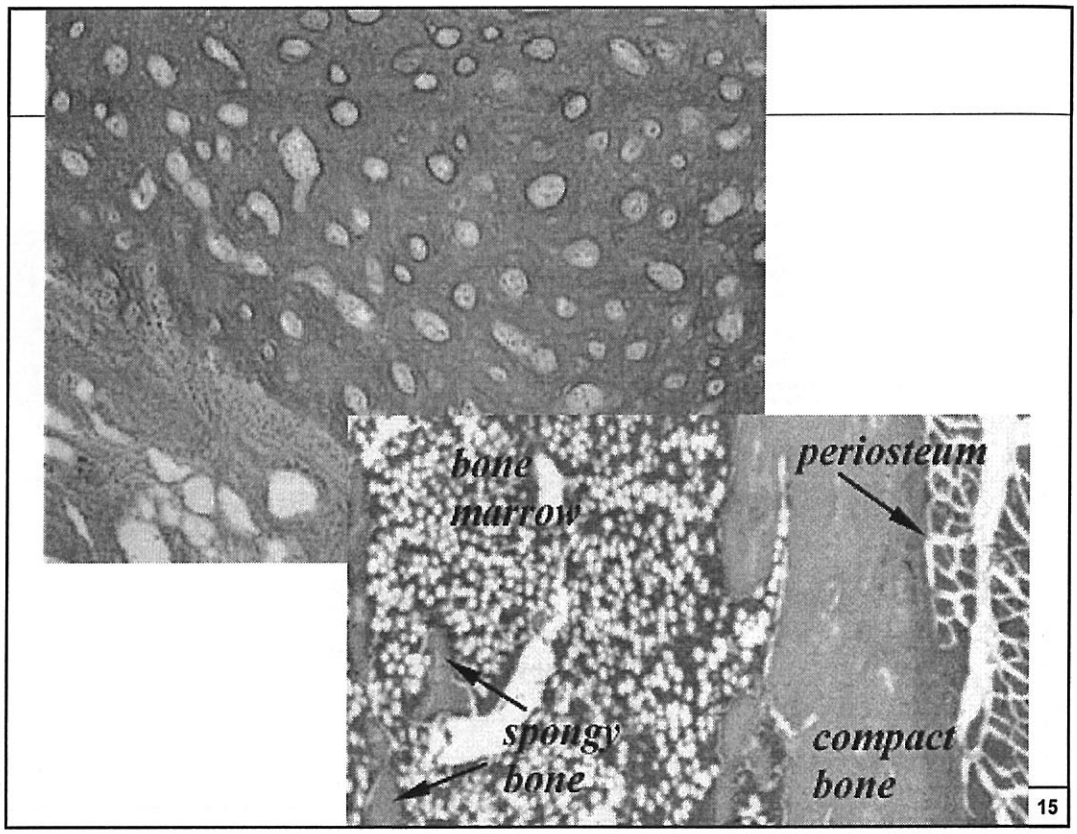
Bone Architecture

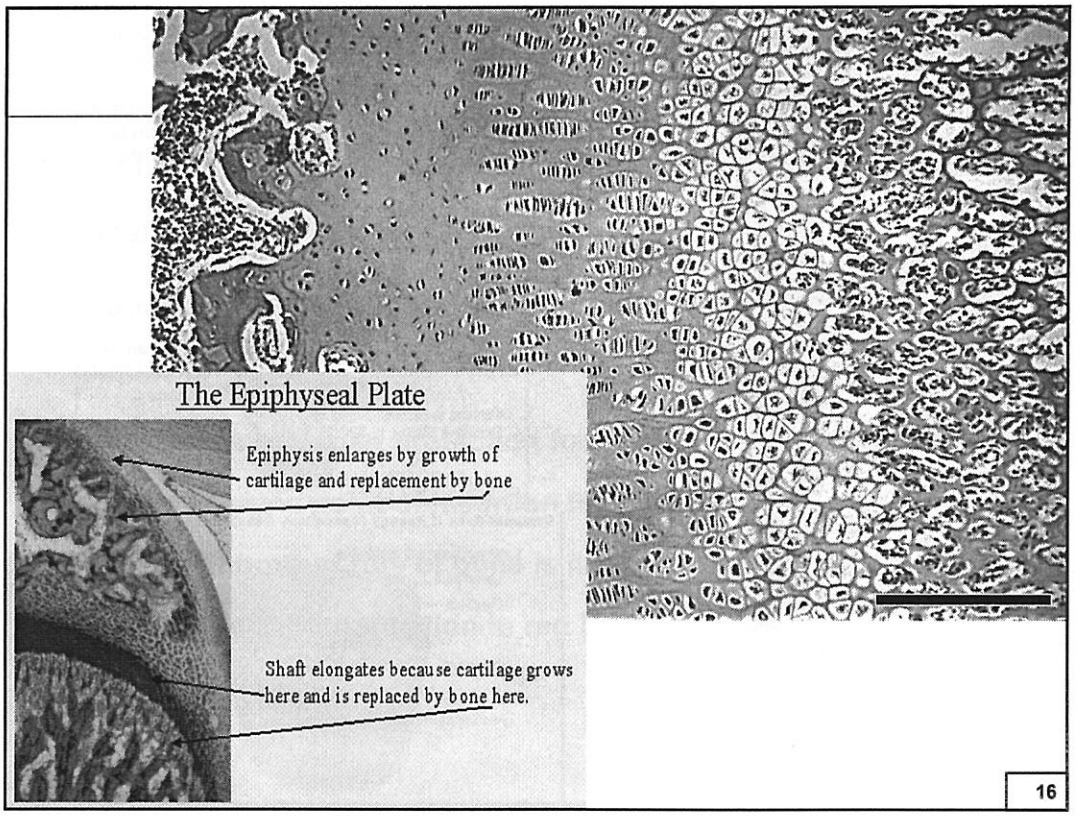




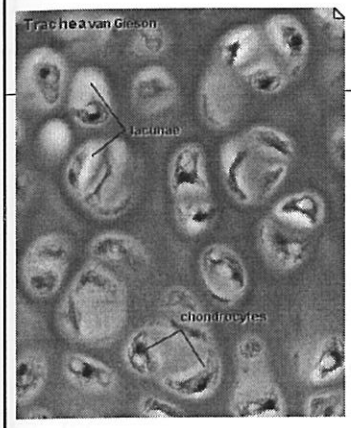





bone marrow
periosteum
spongy bone
compact bone
15

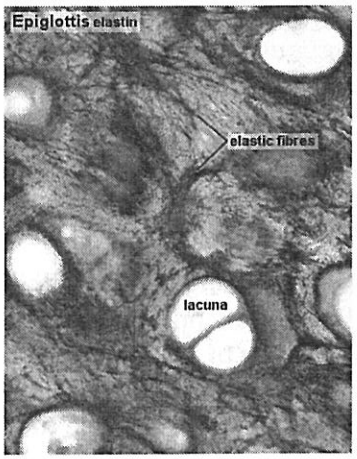

The Epiphyseal Plate
Epiphysis enlarges by growth of cartilage and replacement by bone
Shaft elongates because cartilage grows here and is replaced by bone here.
16

Cartilages

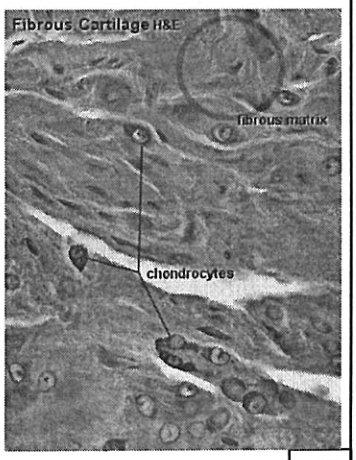


Hyaline cartilage

Elastic cartilage



Fibrous cartilage



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Joints

- A need for strength makes the bones rigid, but if the skeleton consisted of one solid bone, movement would be impossible.
- Nature has solved this problem by dividing the skeleton into many bones and creating joints where the bones intersect. Joints come in a variety of designs, each especially built for the limb it serves.
- Joints permit bodily movement and are held together by fibers called "ligaments". Joints are "oiled" continuously to prevent friction.
- the site of junction or union between bones, especially one that allows motion of the bones.

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There are three main different types of joint.

- **Immovable or Fibrous joints**
  These are very stable and allow no observable movement. Bones are often joined by strong fibres called sutures; eg, the sutures of the cranium.

- **Slightly movable joints or Cartilaginous**
  A cartilaginous joint allows some slight movement. The ends of bones, which are covered in articular or hyaline cartilage, are separated by pads of white fibrocartilage and slight movement is made possible only because the pads of cartilage compress.
  In addition, the pads of cartilage act as shock absorbers.
  The intervertebral discs are examples of this type of joint.

- **Freely movable joints or Synovial joints**
  A synovial joint is a freely moving joint, and is the most common type of joint in the body, and the most important in terms of physical activity, since they allow a wide range of movement. These types of joint are divided up according to the movement that they make possible.
  Surrounding the joint is a membrane called the Synovial Membrane which is where Synovial fluid is formed. This fluid acts as a lubricator and is formed within the joint AND allows friction free movement.
  A good example of this is the knee joint.

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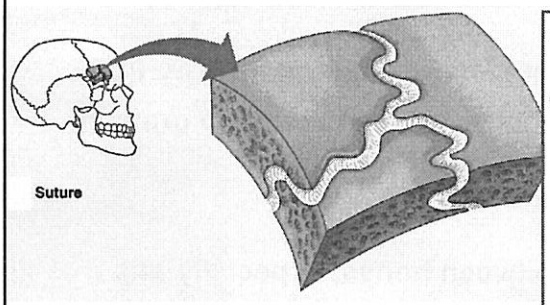
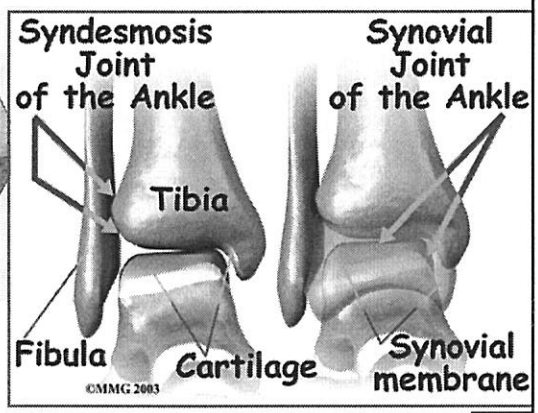
Joints

- **Suture Joint**

  Articulating bones are held together with a band of fibrous connective tissue.

- **Syndesmosis Joint**
  A syndesmosis occurs where there is much more fibrous connective tissue than in a suture, and so the fit between the bones is not so tight.





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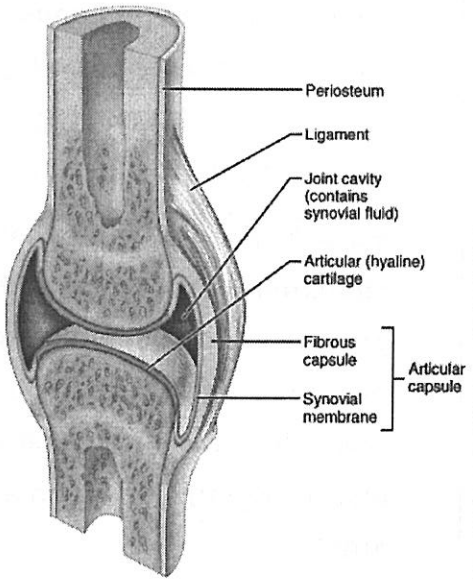
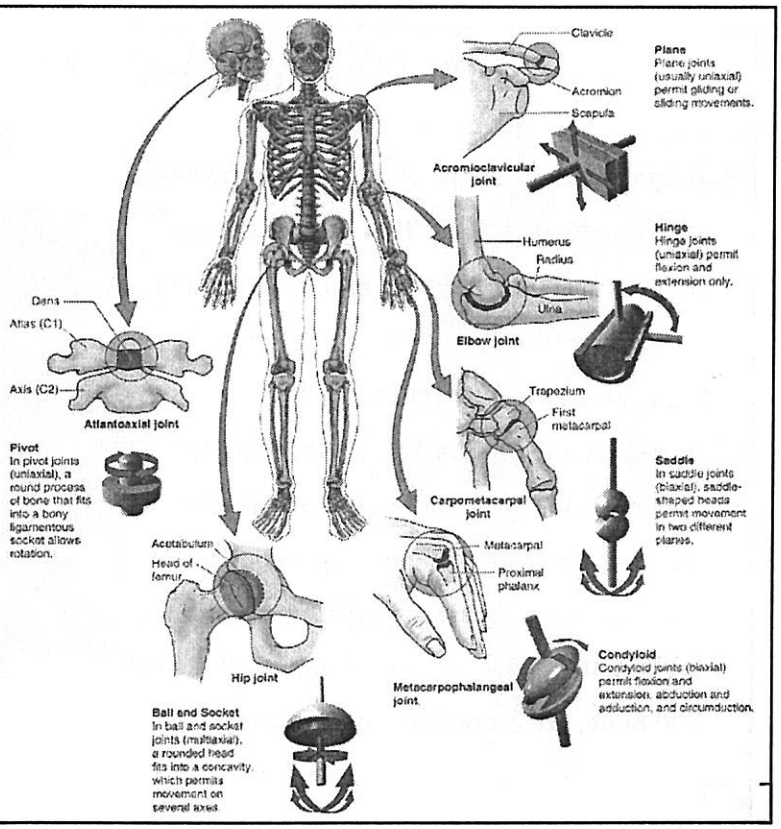
A typical synovial joint

- has four main featues:
- *joint capsule* - the joint enclosure, reinforced by and strengthened with ligaments
- *synovial membrane* - a continuous sheet of connective tissue lining the capsule; its cells produce synovial fluid that lubricates the joint and prevents the two cartilage caps on the bones from rubbing together
- *synovial fluid* - produced by the synovial membrane, the fluid lubricates the joint. In the normal joint, very little fluid (less than 5cc) exists in the cavity.
- *hyaline (articular) cartilage* - where the bones actually "meet"



Types of Synovial Joints

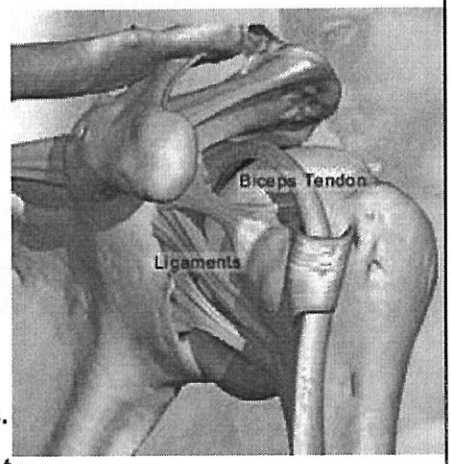


Tendons and Bursas

- Tendons are tough bands of connective tissue made up mostly of a rigid protein called collagen. Tendons firmly attach each end of a muscle to a bone. They are often located within sheaths, which are lubricated to allow the tendons to move without friction.
- Bursas are small fluid-filled sacs that can lie under a tendon, cushioning the tendon and protecting it from injury. Bursas also provide extra cushioning to adjacent structures that otherwise might rub against each other, causing wear and tear—for example, between a bone and a ligament or a bony prominence and overlying skin (such as in the elbow, kneecap, or shoulder area).

Ligaments

- A ligament is a tough band of white, fibrous, slightly elastic tissue. This is an essential part of the skeletal joints; binding the bone ends together to prevent dislocation and excessive movement that might cause breakage. Ligaments also support many internal organs; including the uterus, the bladder, the liver, and the diaphragm and helps in shaping and supporting the breasts. Ligaments, especially those in the ankle joint and knee, are sometimes damaged by injury.



Musculoskeletal System

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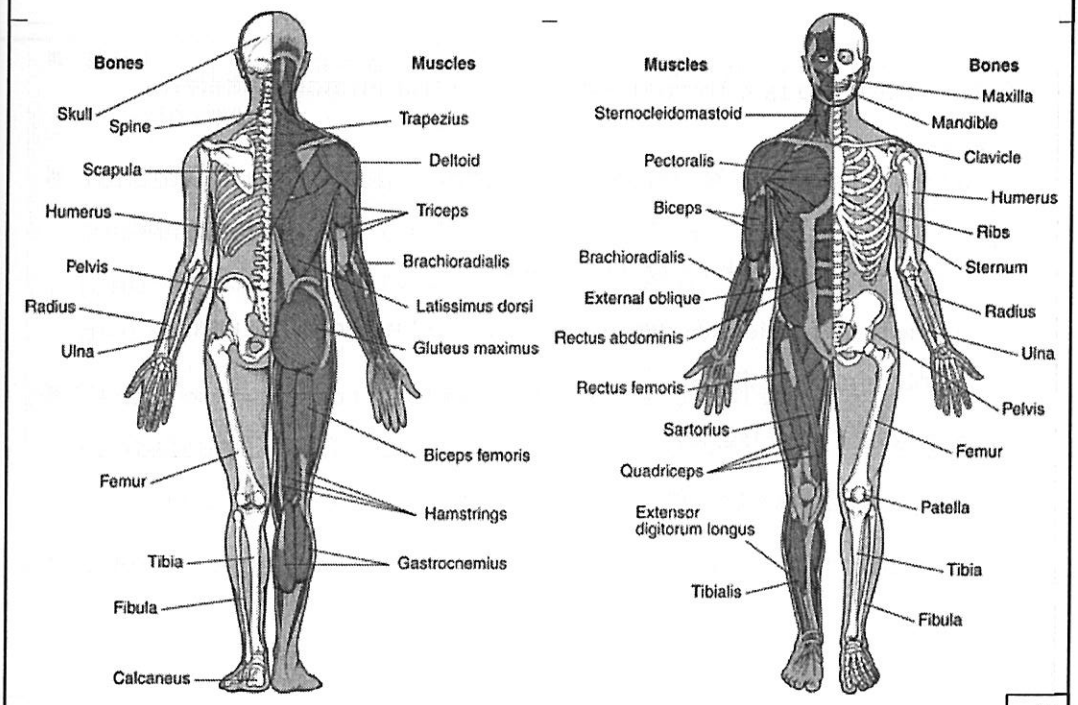
Musculoskeletal System



26

Musculoskeletal System

- The musculoskeletal system consists of the skeletal system -- bones and joints (union of two or more bones) -- and the *skeletal* muscle system (voluntary or striated muscles).
- These two systems work together to provide basic functions that are essential to life, including:
  - Protection: protects the brain and internal organs
  - Support: maintains upright posture
  - Blood cell formation: *hematopoiesis*
  - Mineral homeostasis
  - Storage: stores fat and minerals.
  - Leverage: A lever is a simple machine that magnifies speed of movement or force. The levers are mainly the long bones of the body and the axes are the joints where the bones meet.

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Musculoskeletal System

- There are 5 basic tissues comprising the musculoskeletal system:
  - bones,
  - ligaments (attaching bone to bone)
  - cartilage (protective gel-like subtance lining the joints and intervertebral discs),
  - skeletal muscles, and
  - tendons (attaching muscle to bone).

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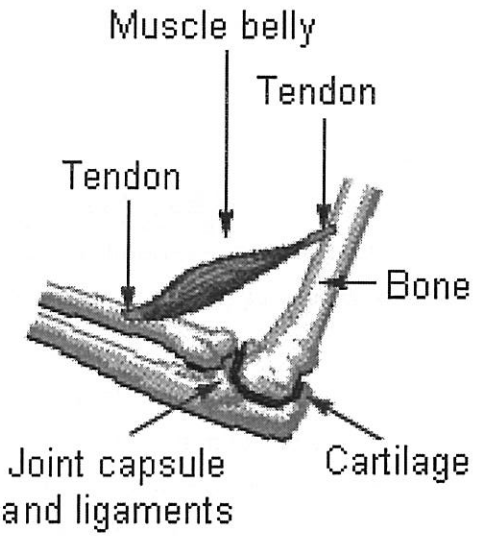
Musculoskeletal System

- Muscles generate force; tendons transfer it to bones; and the bones move if enough force is transmitted. The force must be enough to overcome the weight of the moving body part, gravity, and other external resistance. Motion occurs at joints associated with one or both ends of the bone.



Modified from: DeLisa, Stolov, p. 30

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Musculoskeletal System

- The force is produced in the muscle belly, which consists of muscle tissue.
- Tendons are basically connected bundles of collagen. They are classified as dense regular connective tissue and arise partially from the connective tissue coverings of muscle fibers and fiber groups.
- Tendons attach to the external membrane of a bone, the periosteum, which covers the bone except at joint surfaces. A few muscles bypass tendons and attach directly to the periosteum.
- Other muscles attach to skin (muscles of facial expression),

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Medical Correlations

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Musculoskeletal disorders

- Musculoskeletal disorders include sprains, strains, inflammation, degeneration, tears, pinched nerves or blood vessels, bone splintering and stress fractures.
- Symptoms are discomfort, pain, fatigue, swelling, stiffness, or numbness and tingling.
- Other terms for musculoskeletal disorders
- Cumulative trauma disorders (CTDs) repetitive trauma disorders repetitive strain injuries (RSIs) Repeated motion disorders over use syndromes.

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Skeletal Disorders

- Injury, degenerative wear and tear, and inflammatory disorders affect joints. Sprains are common injuries that cause ligaments to rip of separate from the bone. Tendinitis (such as tennis elbow) and bursitis are inflammations of the tendon sheaths.
- Osteoarthritis is a degenerative condition associated with the wearing away of the protective caps of cartilage covering the bone-ends. Bony growths or spurs develop as the cartilage degenerates, causing restriction of movement and pain. The cause is not known and may just be wear-and-tear associated with aging.
- Rheumatoid arthritis is a severely damaging arthritis that begins with inflammation and thickening of the synovial membrane followed by bone degeneration and disfigurement. More women than men are affected. There may be a genetic predisposition to rheumatoid arthritis. Joint replacement may in some cases restore function.

Osteoporosis

- Osteoporosis is a condition in which a progressive decrease in the density of bones weakens the bones, making fractures likely.
- Aging, estrogen deficiency, low vitamin D or calcium intake, and certain disorders can decrease the amounts of the components that maintain bone density and strength.
- Fractures, particularly of the back, hip, or wrist, can occur with little or no force.
- Some people never develop symptoms, whereas others develop severe sudden pain or gradually develop aching bone pain and deformities.
- Doctors diagnose people at risk by testing their bone density.
- Osteoporosis can be prevented and treated by ensuring adequate calcium and vitamin D intake, engaging in weight-bearing exercise, and taking bisphosphonates or other drugs.

Arthritis

- Arthritis is the inflammation of a joint, and people who have it experience swelling, warmth, pain, and often have trouble moving.
- Although we often think of arthritis as a condition that affects only older people, arthritis can also occur in children and teens.
- Health problems that involve arthritis in kids and teens include juvenile rheumatoid arthritis (JRA), lupus, Lyme disease, and septic arthritis (a bacterial infection of a joint).

Fracture

- A fracture occurs when a bone breaks; it may crack, snap, or shatter.
- After a fracture, new bone cells fill the gap and repair the break.
- Applying a strong plaster cast, which keeps the bone in the correct position until it heals, is the usual treatment.
- If the fracture is complicated, metal pins and plates can be placed to better stabilize it while the bone heals.

Osgood-Schlatter disease(OSD)

1. Osgood-Schlatter disease is an inflammation (pain and swelling) of the bone, cartilage, and/or tendon at the top of the shinbone, where the tendon from the kneecap attaches.
2. OSD usually strikes active teens around the beginning of their growth spurts, the approximately 2-year period during which they grow most rapidly.

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Osteomyelitis

- Osteomyelitis is a bone infection often caused by *Staphylococcus aureus* bacteria, though other types of bacteria can cause it, too.
- In kids and teens, osteomyelitis usually affects the long bones of the arms and legs.
- Osteomyelitis often develops after an injury or trauma.

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PowerPoint

เรื่อง

Hematopoietic System

รองศาสตราจารย์ ดร. กรกช อินทราพิเชฐ

Hematopoietic system

Blood & Bone Marrow

Blood

- Connective tissue with liquid matrix (plasma)
- Cells and cell fragments are also called formed elements
- Flows within cardiovascular system (heart and blood vessels)
- Blood volume
  - 71 ml/kg (70 kg adult male would have about 5,000 ml total blood volume)
- Blood composition is
  - 55% plasma and
  - 45% formed elements or blood cells

Functions of blood

- Primary functions
  - Transportation of molecules within the internal fluid environment
  - Exchange between tissues and between internal/external environment
- Secondary functions
  - Immunity = defense
  - Thermoregulation = radiator fluid
  - Fluid volume homeostasis
  - pH homeostasis

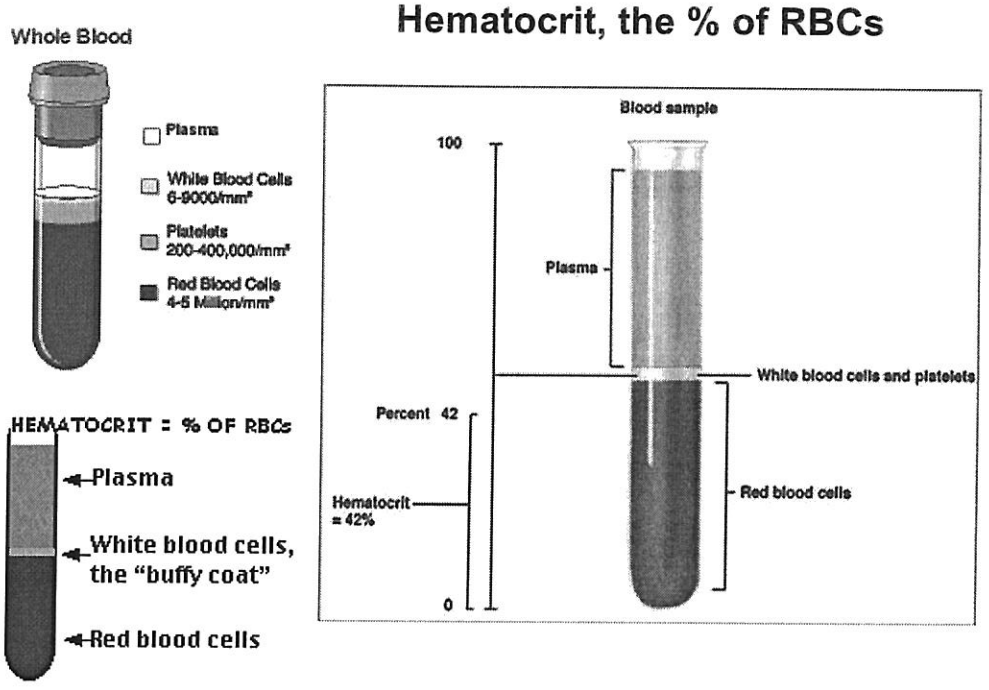
3

Hematocrit or Packed Cell Volume (PCV)

- A "hematocrit" is also known as, relates the volume of red blood cells (RBC's or erythrocytes) to the total blood volume.
- Upon centrifugation, the formed elements settle to the bottom of the tube as
  - 44% a red precipitate or total red blood cell volume as the hematocrit
  - 1% buffy coat of white blood cells and platelets
  - 55% plasma on top as the supernatant.

4

Hematocrit, the % of RBCs



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Hematocrit variation

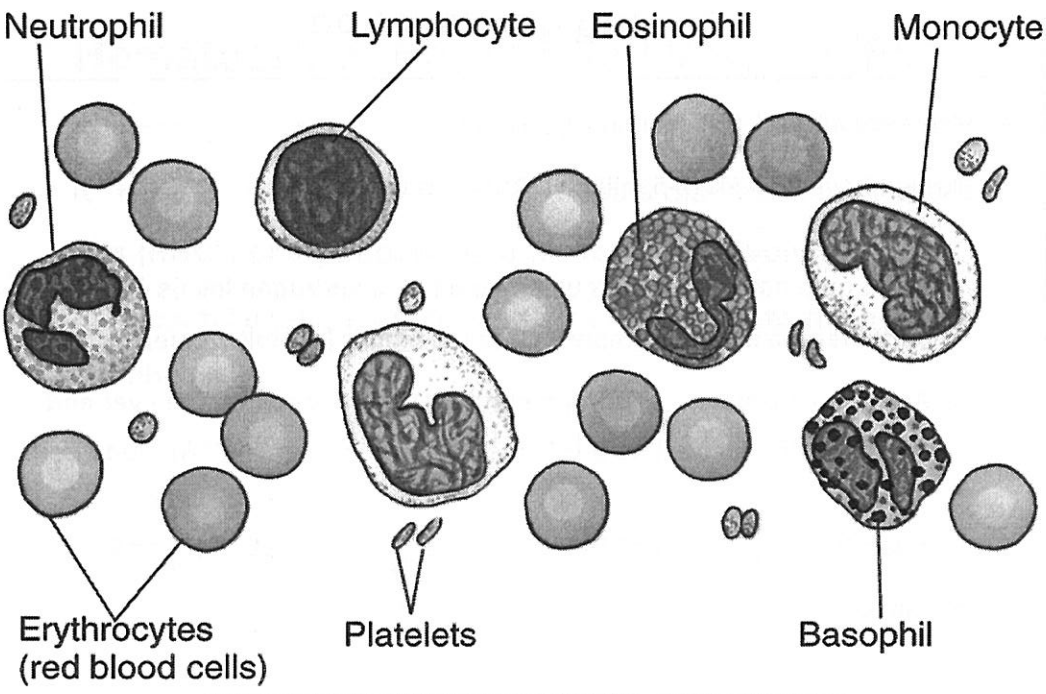
- Men have 40-50% (5-6 million RBC's/mm3)
- Women have 35-45% (4-5 million RBC's/mm3)
  - Adult men have higher circulating bioactive androgen levels (eg. testosterone is approximately 40 times higher in adult women.
  - Androgens promote erythropoietin (EPO) production by the liver and kidneys, that stimulates production of hemoglobin and red blood cells.
- Hematocrits in newborn children (neonates) vary from 40 - 65% and
- Hematocrits in infants vary from lows from 30% - 70%.

6

Identification of Blood composition

- Identification of blood cells is based on the colors produced by stains.
- Methylene blue stains acidic cellular components blue, and
- Eosin stains alkaline components pink.
- Azures, substances formed when methylene blue is oxidized, produced reddish blue.

7



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Plasma

- Plasma is a yellowish fluid in which cells, platelets, organic compounds, and electrolytes are suspended and/or dissolved.
- During coagulation, some of the organic and inorganic components leave the plasma to become integrated into the clot.
- The remaining fluid, which no longer has those components dissolved or suspended in it, differs from plasma, is straw-colored, and is known as serum.

Plasma composition

- The major component of plasma is
  - 90% Water
  - 9% Proteins
  - 1% inorganic salts, ions, nitrogenous compounds, nutrients, and gases constitute the remaining

Colloid osmotic pressure

- The fluid component of blood leaves the capillaries and small venules to enter the connective tissue spaces as extracellular fluid, which has a composition of electrolytes and small molecules similar to that in plasma.
- The concentration of proteins in extracellular fluid is much lower than that in plasma.
- It is difficult even for small proteins to traverse the endothelial lining of a capillary.
- Albumin in plasma is chiefly responsible for the establishment of blood's colloid osmotic pressure to maintain normal blood and interstitial fluid volumes.

Proteins in Plasma

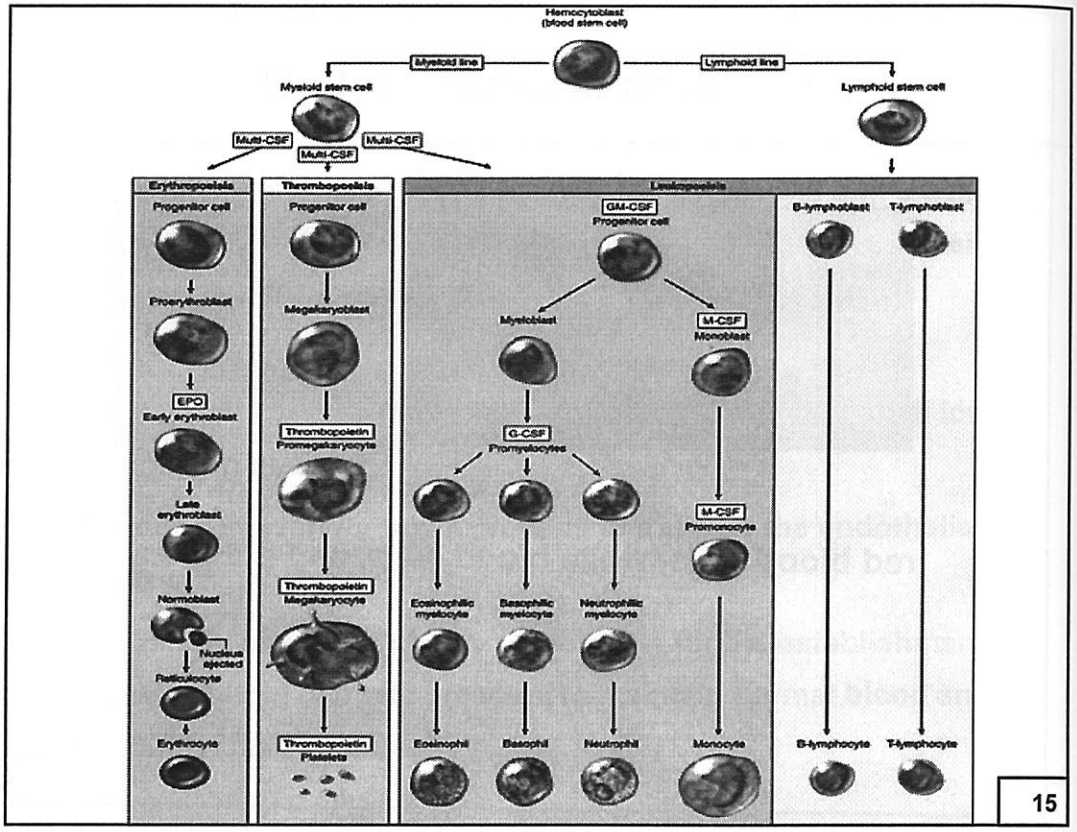
Protein	Function
Albumin	Colloid osmosis & transport of insol metab
Globulins (α-, β-, γ-)	Transport metal ions, lipid sol vit. & Ab
Clotting proteins (eg., prothombin, fibrinogen, accelerator globin)	Forming fibrin threads
Complement proteins (C1 – C9)	Destruction of microbs & inflammation
Plasma lipoproteins Chylomicrond VLDL LDL	 Transport triglycerides to liver Tx triglycerides from liver to body cells Tx cholesterol from liver to body cells

Formed Elements

red blood cells, white blood cells, and platelets

Hemopoiesis / Hematopoiesis

- The finite life span of blood cells requires their constant renewal to maintain a steady circulating population.
- Hemopoiesis is a process of blood cell formation from established blood cell precursors.
- Hemopoiesis = formation of new blood cells
- All are descended from stem cells in red marrow or myeloid tissue.
- Stem cells divide into "lines" of daughter cells, each line producing different groups of blood cells.



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Red Blood Cells / Erythrocytes

- Erythrocytes, the smallest and most numerous cells of blood, have no nuclei and are responsible for
  - the transport of oxygen and carbon dioxide to and from the tissues of the body.
- Each erythrocyte resembles a biconcave-shaped disk
  - 7.5 µm in diameter,
  - 2.0 µm thick at its widest region, and
  - ≤ 1 µm thick at its center.
- This shape provides the cell with a large surface area relative to its volume, thus enhancing its capability for gaseous exchange.
- 4-6 million per cubic mm of blood (RBC count)

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Red Blood Cells / Erythrocytes (cont.)

- Erythrocytes' cytosol possess
  - no organelles
  - have soluble enzymes
- Carbonic anhydrase facilitates the formation of carbonic acid from CO_2 and water.
  - This acid dissociates to form bicarbonate (HCO_3^-) and hydrogen (H^+).
  - It is as bicarbonate that most of the CO_2 is ferried to the lungs for exhalation.
- Hemoglobin and contain lipoprotein stroma.
  - in hypotonic solution, they become spherical, and hemogolbin escapes and is dissolved in the surrounding liquid, called hemolysis.
- The membrane of empty shell is called ghost.

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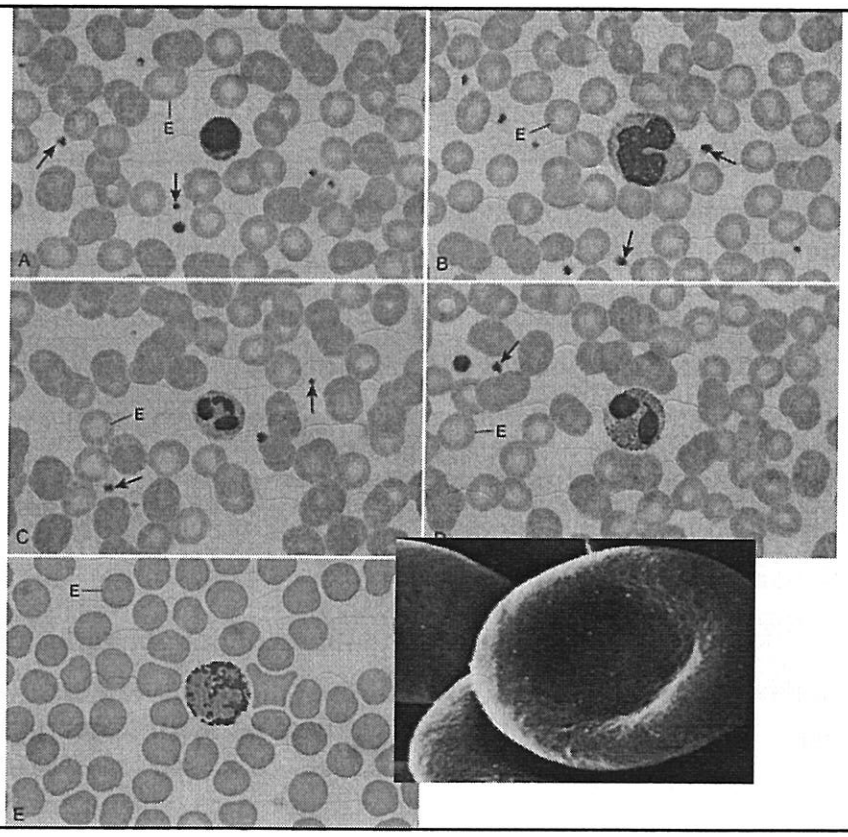

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Red Blood Cells / Erythrocytes (cont.)

- Size of RBC with
  - diameter $\geq$ 9 μm are called macrocytes
  - diameter $\leq$ 6 μm are called microcytes.
- The presence of high percentage of erythrocytes of abnormal variation in size is called anisocytosis.

Hemopoiesis of Erythrocytes

- Erythrocyte precursor cells within the bone marrow possess nuclei.
- During development and maturation the precursor cells or erythrocytes expel their nuclei and organelles before entering the circulation, so that the mature erythrocytes have no nuclei.
- Human erythrocytes have an average life span of 120 days; when they reach that age, they display on their surface a group of oligosaccharides.
- Red blood cells at old age bearing these oligosaccharides groups are destroyed by macrophages of the spleen, bone marrow, and liver.

Hemoglobin

- Red blood cells are packed with hemoglobin, a large tetrameric protein (68,000 Da) of hemoglobin.
- Hemoglobin is composed of four polypeptide chains, each of which is covalently bound to an iron-containing heme.
- Heme molecule is bound within a hydrophobic depression, the heme pocket, of the globin chain which protects the iron from being oxidized while permitting the binding of oxygen to it.

Hemoglobin (cont.)

- This property of hemoglobin is conveyance of respiratory gases.
- Hemoglobin carrying O_2 is known as oxyhemoglobin, and
- Hemoglobin carrying CO_2 is called carbaminohemoglobin or carbamylhemoglobin.
- Hypoxic tissues release 2,3-diphosphoglyceride, a carbohydrate that facilitates the release of oxygen from the erythrocyte.
- Hemoglobin also binds nitric oxide (NO), a neurotransmitter substance that causes dilation of blood vessels, permitting red blood cells to release more oxygen and pick up more CO_2 within the tissues of the body.

Hemoglobin structure

- Hemoglobin molecule is a quaternary protein of four globular protein subunits.
  - 2 of α subunits
  - 2 of β subunits
- Each subunit is composed of a protein chain tightly associated with a non-protein heme group.
- Each protein chain arranges into a set of alpha-helix structural segments connected together in a globin fold arrangement.
- This folding pattern contains a pocket which strongly binds the heme group.

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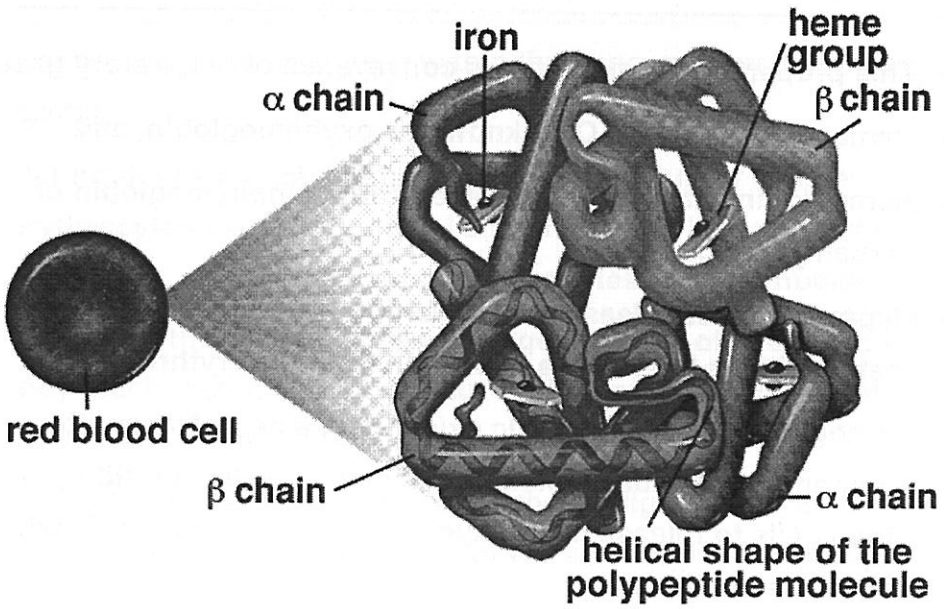
Hemoglobin Molecule



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Hemoglobin Disorders

- Normocytic anemia are average sized red blood cells.
- Microcytic anemia is the most frequent form of anemia. Individuals afflicted with microcytic usually appear pale. Iron deficiency is one of the causes of anemia since iron is a vital part of hemoglobin function.
- Macrocytic anemia can be cause by several factors. Lack of folic acid or vitamin B12, alcoholism and prescription medicine that inhibit DNA replication

Thalassemia

- Thalassemia is an inherited disorder associated with red blood cells. It is a recessive trait disease where both parents are carriers.
- In thalassemia, a mutation occurs in the hemoglobin gene which results in the decreased rate of normal globin subunit synthesis, an abnormalty in the chains of the protein,
- There are two forms of thalassemias:
  - ß thalassemia and
  - α thalassemia.
- Found 3-14% in Thailand

Sickle-cell anemia

- Sickle-cell disease is a heritable hemoglobin disorder caused by abnormally shaped red blood cells, recessive trait disease
- Red blood cells with abnormal shape can aggregate within blood vessels which can lead to several complications.
- One of them is called Vaso-occlusive crises, aggregate abnormal red blood cells obstruct blood flow to organ tissues.
- This condition can lead to pain and eventual organ damage.
- Frequently found in people of African descent.

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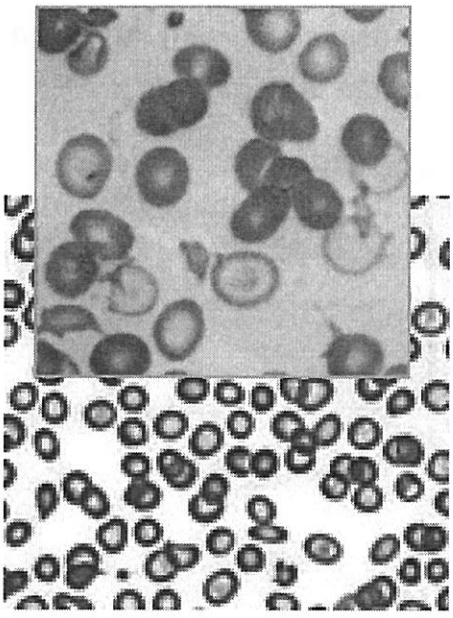
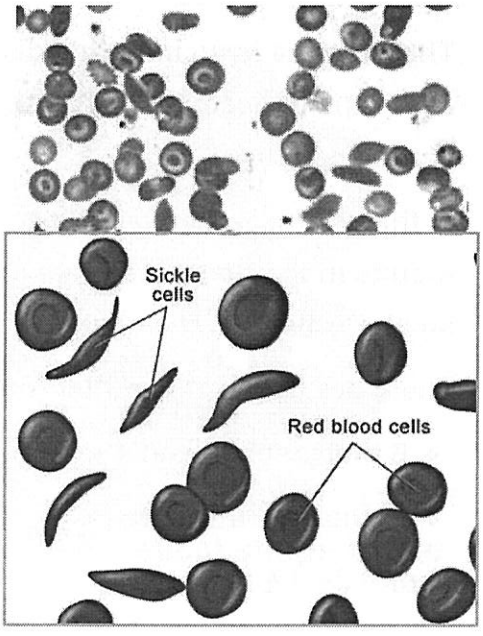
Thalassemia



Sickle cell anemia



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Erythrocyte Cell Membrane

- The red blood cell plasma membrane, a typical lipid bilayer, is composed of about
  - 50% protein,
  - 40% lipids, and
  - 10% carbohydrates.
- The extracellular surface of the red blood cell plasmalemma has specific inherited carbohydrate chains that act as antigens and determine the blood group of an individual for the purposes of blood transfusion.

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Erythrocyte Cell Membrane (cont.)

- The most notable of these are the A and B antigens, which determine the four primary blood groups, A, B, AB, and O.
- People who lack either the A or B antigen, or both, have antibodies against the missing antigen in their blood;
- If they undergo transfusion with blood containing the missing antigen, the donor erythrocytes are attacked by the recipient's serum antibodies and are eventually lysed.

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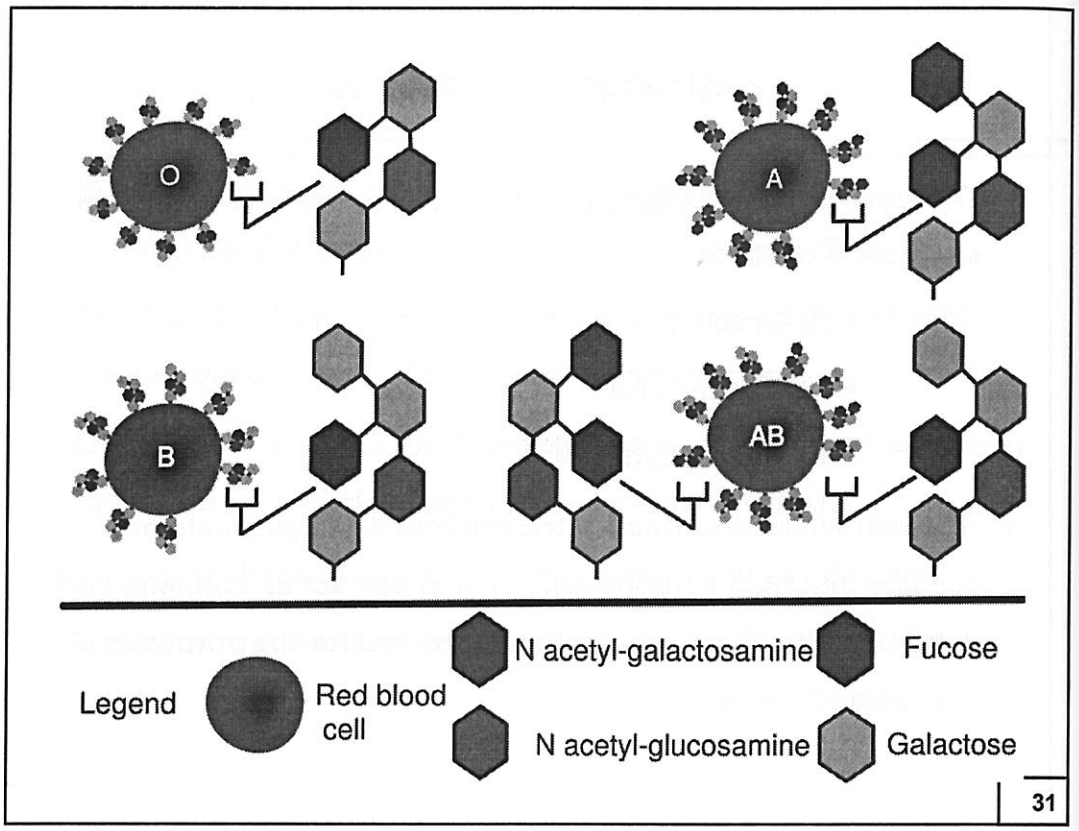
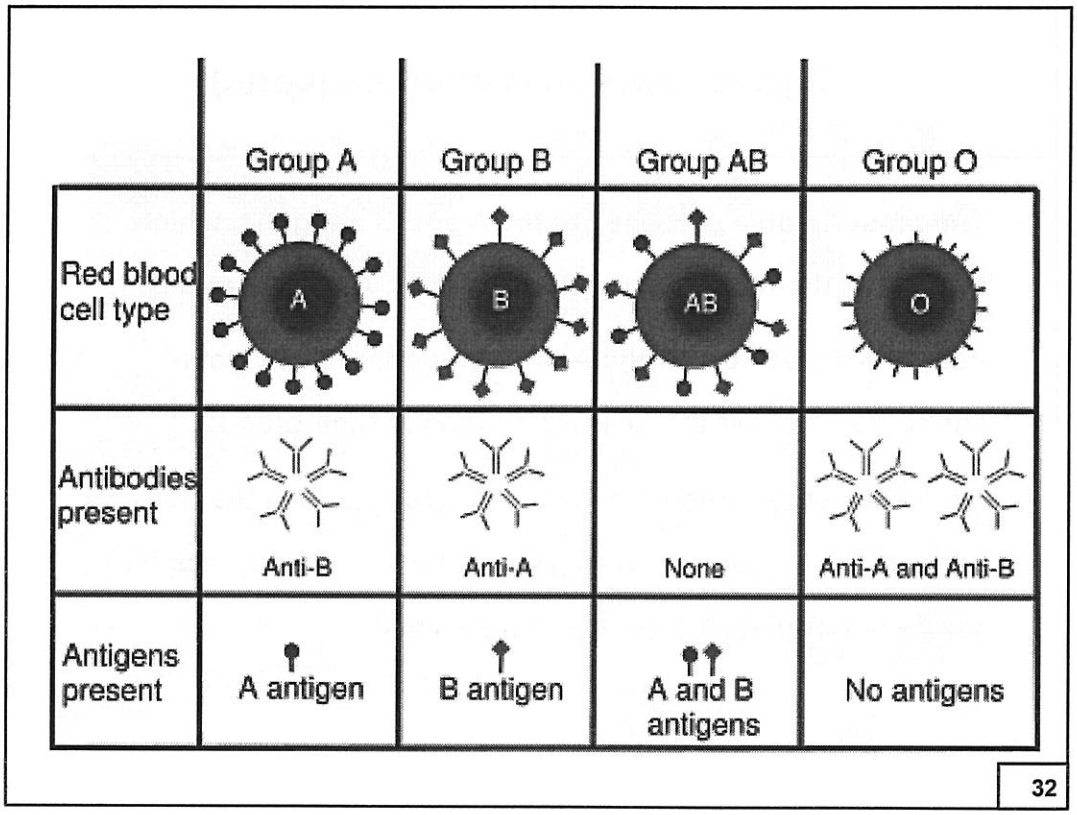

O
A
B
AB
Legend
Red blood cell
N acetyl-galactosamine
Fucose
N acetyl-glucosamine
Galactose

31


Group A
Group B
Group AB
Group O
Red blood cell type
A
B
AB
O
Antibodies present
Anti-B
Anti-A
None
Anti-A and Anti-B
Antigens present
A antigen
B antigen
A and B antigens
No antigens

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Erythrocyte Cell Membrane (cont.)

- Another important blood group, the Rh group, is so-named because it was first identified in rhesus monkeys.
- This complex group comprises more than two dozen antigens, although many are relatively rare.
- Three of the Rh antigens of C, D, and E are so common in the human population that the erythrocytes of 85% of Americans have one of these antigens on their surface,
  - individuals are thus said to be Rh-positive (Rh+).
  - individuals lacking these antigens are RH-negative (RH-).

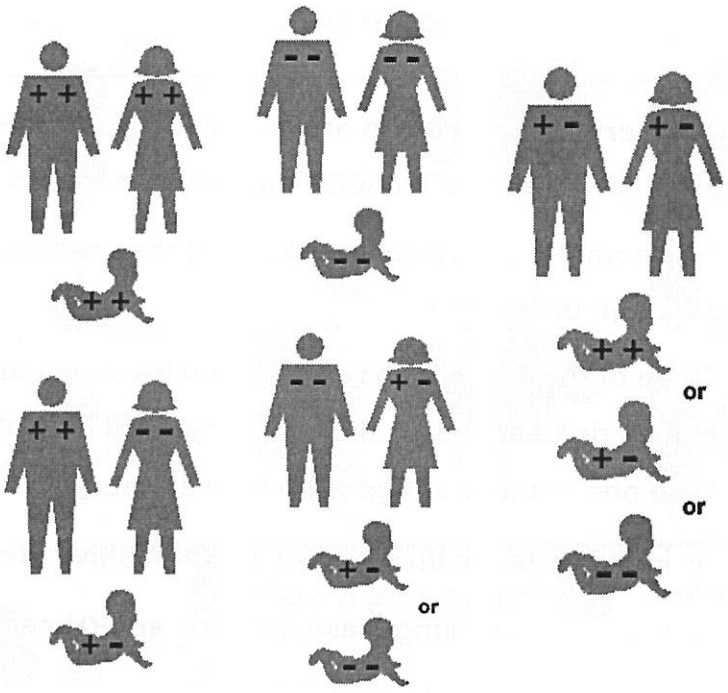
Erythrocyte Cell Membrane (cont.)

- The following are the possible combinations of blood types with the Rh factors:

Blood type	A	B	O	AB
Rh positive	A+	B+	O+	AB+
Rh negative	A-	B-	O-	AB-

- A baby may have the blood type and Rh factor of either parent, or a combination of both parents.
- The Rh positive gene is dominant and even when paired with an Rh negative gene, the positive gene takes over.

Rh factor



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Leukocytes

- Leukocytes are white blood cells that are classified into two major categories: granulocytes and agranulocytes.
- A healthy adult has only 6500 to 10,000 WBC per mm^3 of blood.
- Leukocytes do not function within the bloodstream but use it as a means of traveling from one region of the body to another.
- When leukocytes reach their destination, they leave the bloodstream by migrating between the endothelial cells of the blood vessels, enter the connective tissue spaces, and perform their function, against foreign substances.

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Classification of Leukocytes

White blood cells are classified into two groups:

1. **Granulocytes have granules in their cytoplasm,**
    - **Neutrophils**
    - **Eosinophils**
    - **Basophils**
2. **Agranulocytes, which lack specific granules,**
    - **Lymphocytes**
    - **Monocytes**

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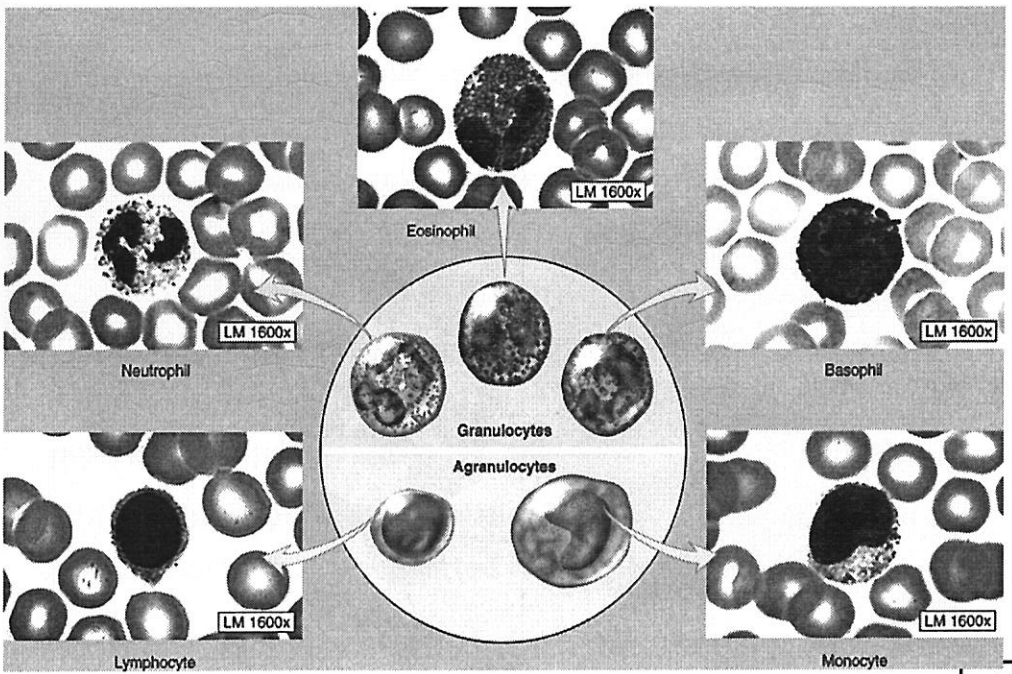
Leukocytes



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Neutrophils

- Neutrophils are polymorphonuclear leukocytes, compose most of the white blood cell population; they are avid phagocytes, destroying bacteria that invade connective tissue spaces using the contents in their granules.
- In females, the nucleus presents a characteristic small appendage, the "drumstick," which contains the condensed, inactive second X chromosome, called the Barr body.
- Neutrophils are among the first cells to appear in acute bacterial infections.
- The neutrophil plasmalemma possesses complement receptors as well as Fc receptors for IgG.

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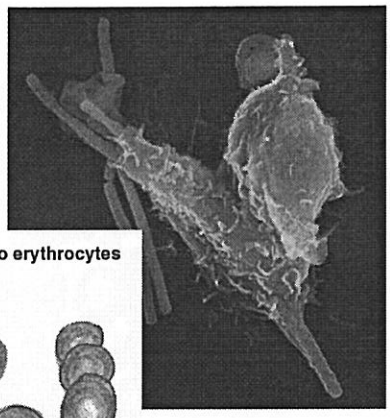
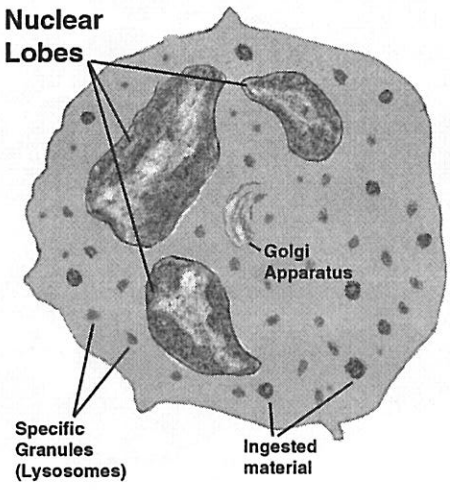
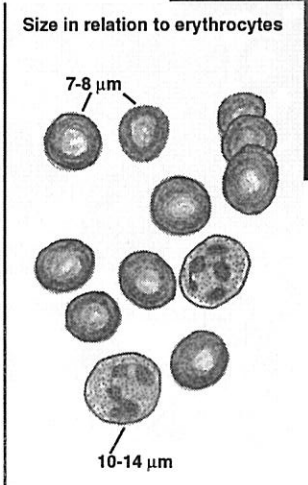
Neutrophil







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Neutrophil granules

- Three types of granules are present in the cytoplasm of neutrophils:
  - Small, specific granules (0.1 µm in diameter)
  - Larger azurophilic granules (0.5 µm in diameter)
  - Tertiary granules.

Neutrophil granules (cont.)

- Specific granules contain various enzymes and pharmacological agents that aid the neutrophil in performing its antimicrobial functions. In electron micrographs these granules appear somewhat oblong.
- Azurophilic granules, as already indicated, are lysosomes, containing acid hydrolases, myeloperoxidase, the antibacterial agent lysozyme, bactericidal permeability-increasing (BPI) protein, cathepsin G, elastase, and nonspecific collagenase.
- Tertiary granules contain gelatinase and cathepsins as well as glycoproteins that are inserted into the plasmalemma.

Eosinophils

- Eosinophils are 10 to 14 µm in diameter, a sausage-shaped, bilobed nucleus. The two lobes are connected by a thin chromatin strand.
- They are round cells in suspension, but they may be pleomorphic during their migration through connective tissue.
- Their cell membrane has receptors for immunoglobulin G (IgG), IgE, and complement.
- Eosinophils are produced in the bone marrow under the control of interleukin-5 (IL-5) to proliferate and differentiate into mature cells.
- Eosinophils phagocytose antigen-antibody complexes and kill parasitic invaders.

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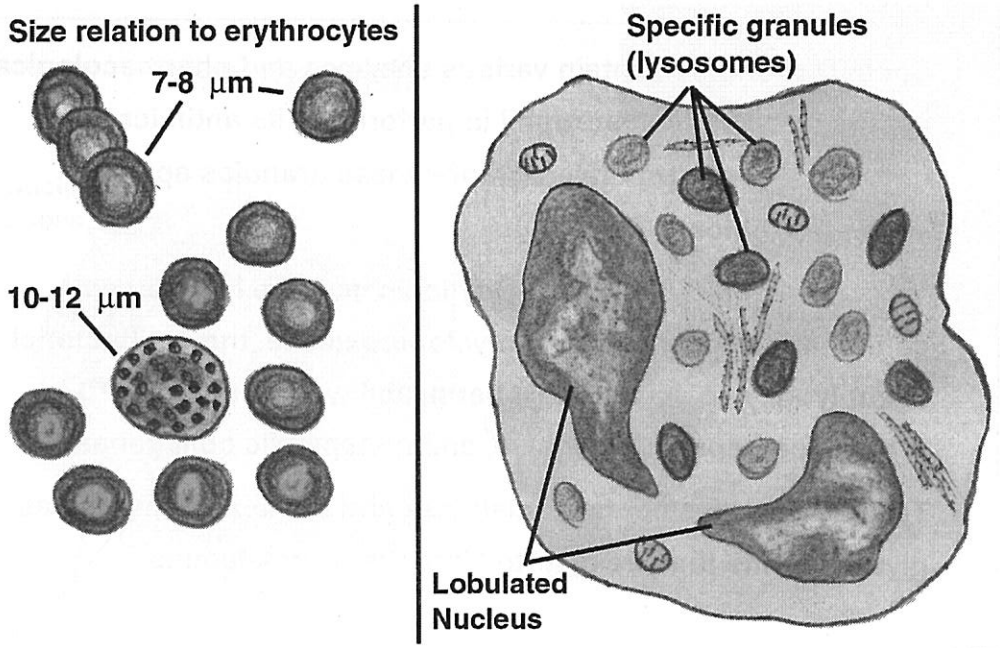
Eosinophil



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Eosinophil granules

- The specific granules of eosinophils possess an externum and an internum
- Specific granules have a crystal-like, electron-dense center or internum, surrounded by a less electron-dense or externum.
  - The internum contains major basic protein, eosinophilic cationic protein, and eosinophil-derived neurotoxin, as efficacious agents in combating parasites.
  - The externum also contains the enzymes
- Nonspecific azurophilic granules are lysosomes containing hydrolytic enzymes, function both in the destruction of parasitic worms and in the hydrolysis of antigen-antibody complexes.

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Basophils

- Basophils are similar to mast cells in function, but different origins.
- They are round cells in suspension but may be pleomorphic during migration through connective tissue.
- They are 8 to 10 µm in diameter, S-shaped nucleus which is commonly masked by the large specific granules in the cytoplasm.
- Basophils have several surface receptors on their plasmalemma, including immunoglobulin E (IgE) receptors (FcεRI).

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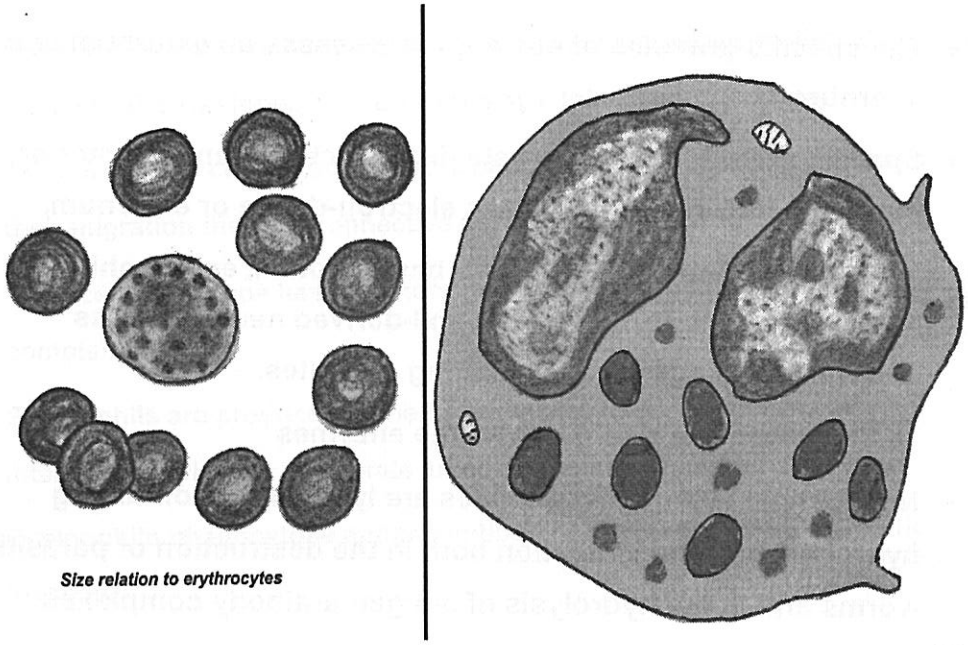
Basophil



Size relation to erythrocytes

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Basophil granules

- Basophils possess specific granules and azurophilic granules
- Specific granules stained dark blue to black with Giemsa and Wright stains, about 0.5 μm in diameter and frequently press against the periphery of the cell, creating the basophil's characteristic "roughened" perimeter, as seen by LM.
- The granules contain heparin, histamine, eosinophil chemotactic factor, neutrophil chemotactic factor, neutral proteases, chondroitin sulfate, and peroxidase.
- Nonspecific azurophilic granules are lysosomes, which contain enzymes similar to those of neutrophils.

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Monocytes

- Monocytes, the largest of the circulating blood cells, enter the connective tissue spaces, where they are known as macrophages.
  - large, acentric, kidney-shaped nucleus that frequently has a "moth-eaten," soap-bubble“
  - chromatin is coarse but not overly dense
  - two nucleoli are present, not always evident in smears.
  - bluish gray cytoplasm
  - numerous azurophilic granules (lysosomes) and occasional vacuole-like spaces

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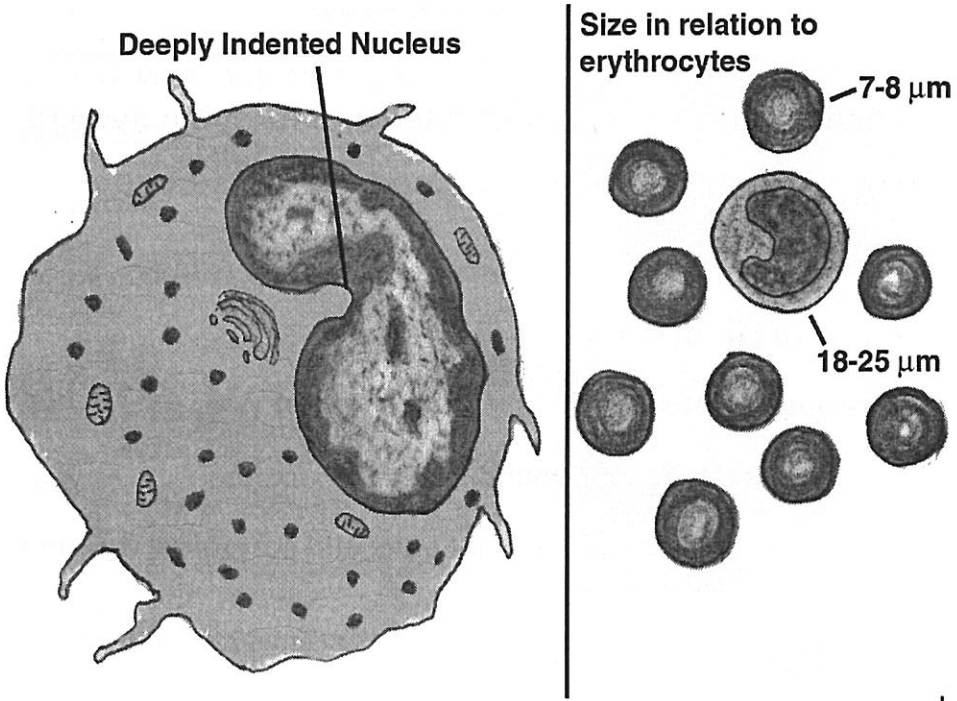
Monocyte



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Monocytes

- Monocytes stay in circulation for only a few days;
  - then migrate through the endothelium of venules and capillaries into the connective tissue, where they differentiate into macrophages.
- Macrophages phagocytose unwanted particular matter.
  - produce cytokines that are required for the inflammatory and immune responses, and
  - present epitopes to T lymphocytes.
  - It is named Antigen-Presenting Cells (APCs).

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Lymphocytes

- Lymphocytes are agranulocytes and form the second largest population of white blood cells.
- Lymphocytes are
  - 8 to 10 μm in diameter and
  - dense nucleus is rich in heterochromatin
    - slightly indented, round, acentric nucleus
- A few azurophilic granules, light blue, and peripheral location.

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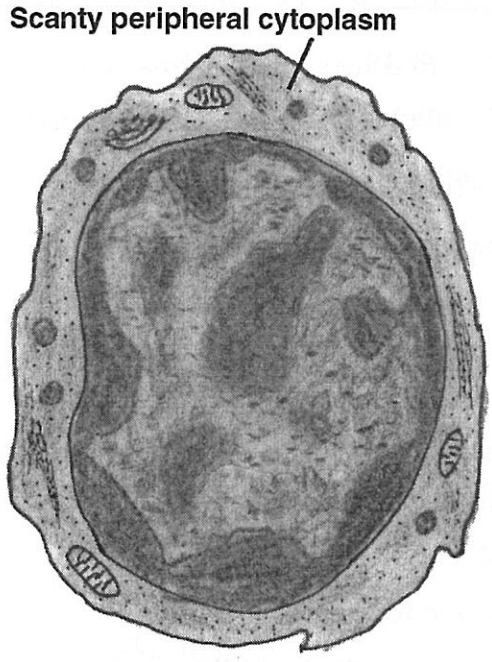
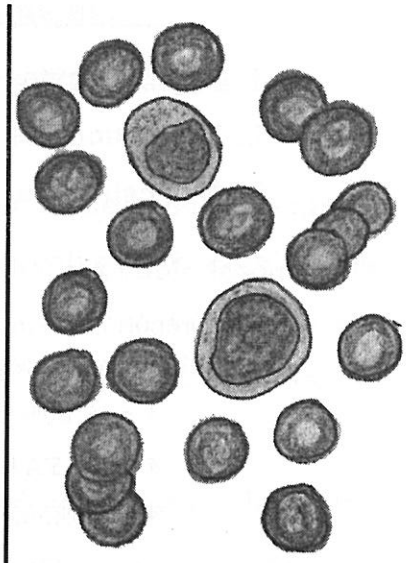
Lymphocyte





Size relation to erythrocytes

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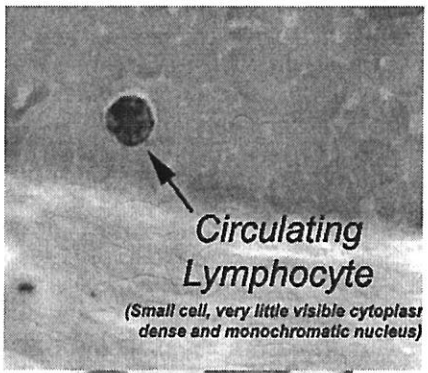
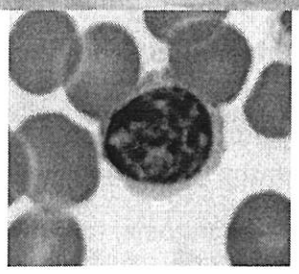
Lymphocytes (cont.)

- Size of lymphocytes may be described as
  - small
    8 - 10 µm ,
  - medium (less)
    12 - 15 µm,
  - large (less)
    15 - 18 µm





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Three Functional Lymphocytes

1. B lymphocytes (B cells)
2. T lymphocytes (T cells)
3. Null cells. (stem cells)

- Their morphology are indistinguishable from each other
  - be recognized immunocytochemically by the differences in their surface markers = Custer of difference = CD.
    - app. 80% T cells in circulation
    - app.15% B cells, and
    - the remainder is null cells.
- Their life spans also differ widely:
  - some T cells may live for years, whereas
  - some B cells may die in a few months.

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- B cells enter as yet unidentified regions of the bone marrow.
- T cells migrate to the cortex of the thymus.
- Lymphocytes :
  - proper functioning of the immune system in connective tissue.
  - migrate to specific body compartments to mature and
  - express specific surface markers and receptors and
  - become immunologically competent.
- Competent lymphocytes
  - leave their respective sites of maturation,
  - enter the lymphoid system, and
  - undergo mitosis, forming a group of identical cells, known as a clone.

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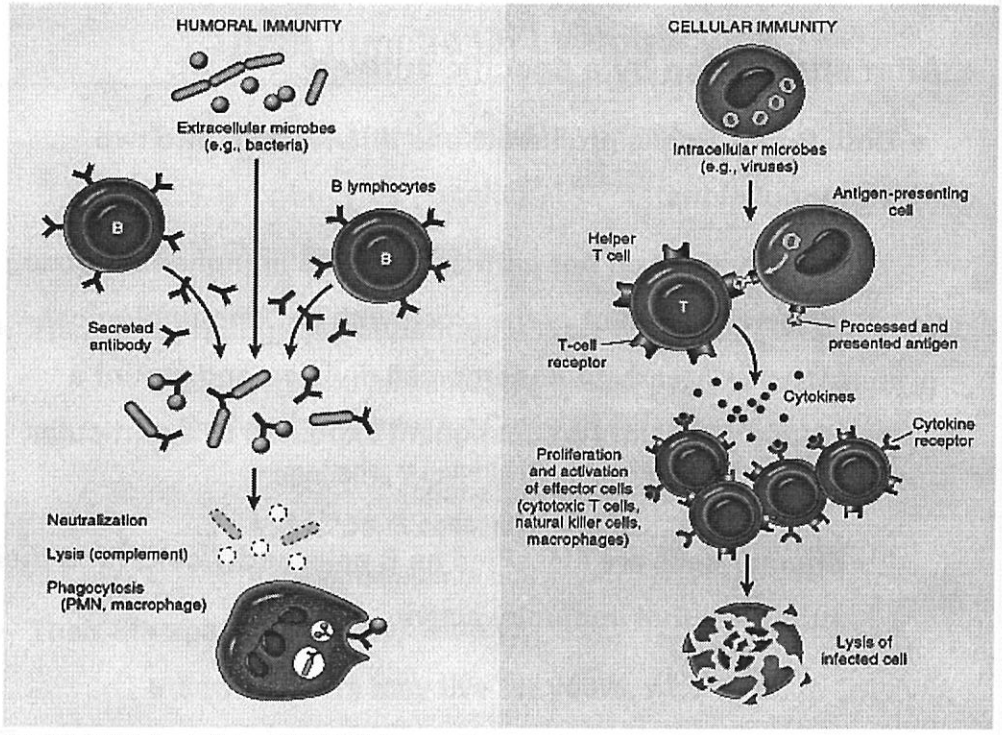
- **After stimulation by a specific antigen:**
  - **Both B and T cells proliferate and differentiate into two subpopulations:**
    - **Memory cells do not participate in the immune response but remain as part of the clone with an "immunological memory," ready to undergo cell division and mount a response against a subsequent exposure to a particular antigen or foreign substance.**
    - **Effector cells are classified as B cells and T cells (and their subtypes) that immunity active.**

Effector cells

- **Immunocompetent lymphocytes that can perform lymphocyte immune functions, = eliminating antigens.**
  - **B cells differentiate into plasma cells**
    - **responsible for the humorally mediated immune system, which produce antibodies against antigens.**
  - **T cells differentiate into many subtypes**
    - **responsible for the cellularly mediated immune system.**



Some T cells differentiate into;

- Cytotoxic T cells (CTLs; T killer cells), which make physical contact with and kill foreign or virally altered cells.
- Helper T cells are responsible for the initiation and development of B cells
- Regulatory T cells (T suppressor cells) for the suppression of most humorally and cellularly mediated immune responses. They accomplish this by releasing signaling molecules known as cytokines (lymphokines) that elicit specific responses from other cells of the immune system
- Natural killer T (NKT) cells are a heterogeneous group of T cells that share properties of both T cells and Natural killer (NK) cells. They recognize the non-polymorphic CD1 molecule, an antigen-presenting molecule that binds self- and foreign lipids and glycolipids.

Null cells

- Lymphocytes that develop in the bone marrow
- Lack the characteristic surface markers of the B and Tcells.
- Capable of lysing a variety of tumor or virus infected cells and cancer cells.
- Composed of two distinct populations:
  - Circulating stem cells, which give rise to all of the formed elements of blood
  - Natural killer (NK) cells, which can kill some foreign and virally altered cells without the influence of the thymus or T cells.
- *Natural killer (NK) cells should not be confused with Natural killer T (NKT) cells.*

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Platelets

- Platelets (thromboplastids) are small, disk-shaped, non-nucleated cell fragments derived from megakaryocytes in the bone marrow.
- Platelets are about 2 - 4 μm in diameter in blood smears.
- In light micrographs, they display
  - a peripheral clear region, the hyalomere, and
  - a central darker region, the granulomere.
- The platelet plasmalemma has numerous receptor molecules and glycocalyx (15 - 20 nm thick) .
- There are between 250,000 - 400,000 platelets per mm^3 of blood, with a life span of $\leq$ 14 days.

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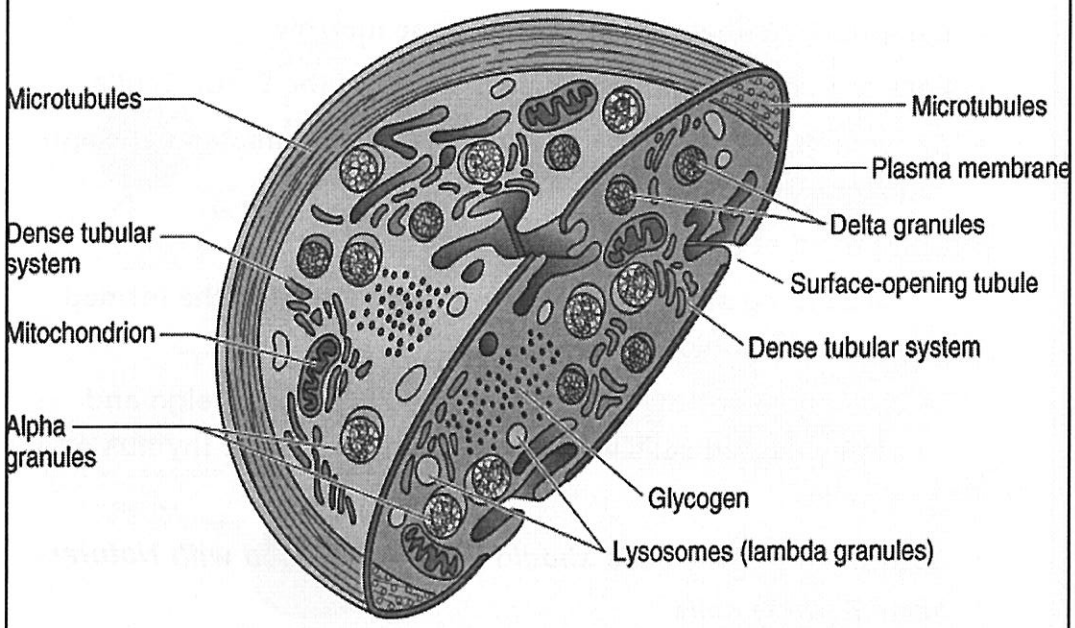
Platelet



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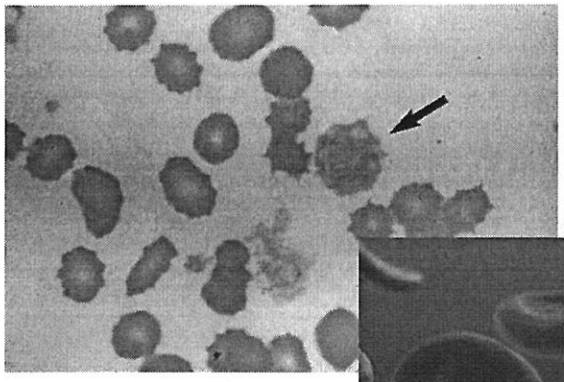
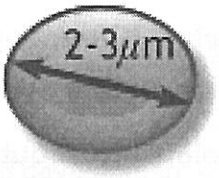
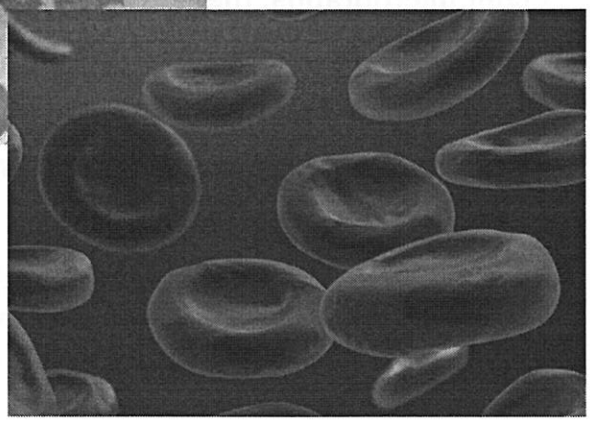
Platelet







RBC

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Platelet composition

- Platelets possess
  - Hyalomere – tubular system
  - Granulomere – membrane bound granules

Hyalomere of Platelet

- Platelets contain two tubular systems;
  - dense tubular system and
  - surface opening or open canalicular system.
    - Around the periphery of the platelet lies a marginal bundle of microtubule; this bundle helps to maintain the platelet's ovoid shape.
- Actin and myosin in hyalomere can assemble to form a contractile system that functions in platelet movement and aggregation.
- A cell coat for platelet adhesion, rich in glycoaminoglycans and glycoproteins, 15-20 nm thick.

Hyalomere of Platelet (cont.)

1. The open canlicular system, that connects to invaginations of the platelet plamalemma. This arrangement is probably of functional significance in facilitating the liberation of active molecules stored in platelets. the luminal aspect of this tubular system is a continuation of the outer surface of the platelet, thus increasing the platelet surface area by a factor of 7 - 8.
2. The dense tubular system is electron-dense irregualar tubes.

Granulomere of Platelet

- The central granulomere possessed a variety of membrane-bound granules and a sparse population of mitochondria and glycogen particles.
  - α granule : contain fibrinogen, platelet-derived growth factor and other specific proteins
  - δ granule : contain calciumions, pyrophosphate, adenosine diphosphate (ADP), and adenosine triphosphate (ATP)
  - λ granule : contain only lysosomal enzymes.

Platelet Function

The role of platelets in controlling hemorrhage to the endothelial lining of the blood vessel in case of injury;

- Primary aggregation - to the exposed collagen, via collagen-binding protein in platelet membrane.

  A platelet plug is formed as a first step to stop bleeding.

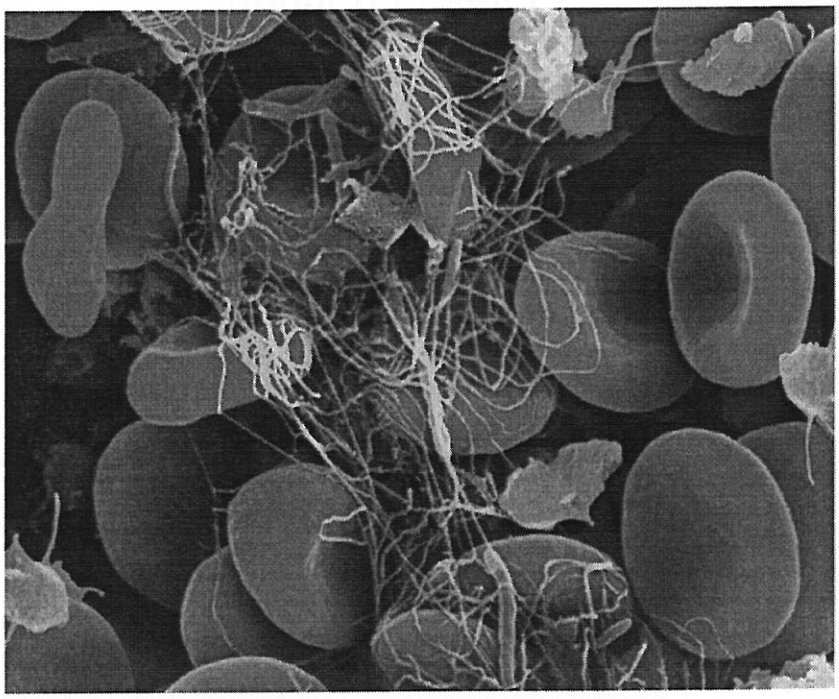
- Secondary aggregation – platelets in the plug release an adhesive glycoprotein and ADP to induce aggregation.

  This increases the size of platelet plug

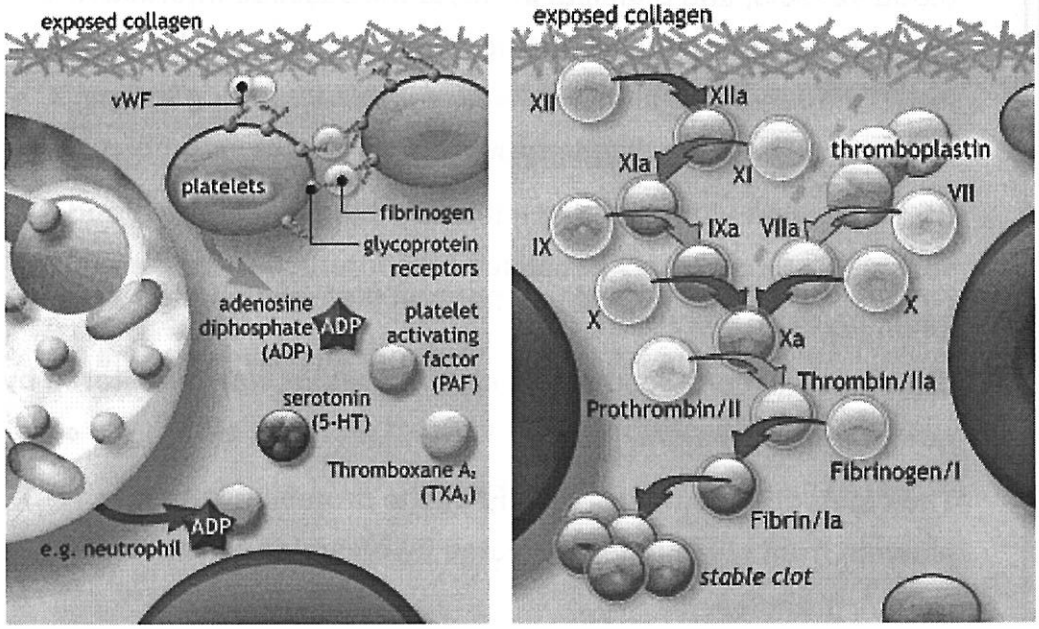
- Blood coagulation – factors from the blood plasma, damaged blood vessels, and platelets promote the cascade interaction of about 13 plasma proteins, giving rise to a polymer, fibrin, that forms a three-dimensional network of fibers trapping red cells, leukocytes, and platelets to form a blood clot, or thrombus
- Clot retraction – the clot that initiatially bulges into the blood vessel lumen contracts because of the interaction on platelet actin, myosin, and ATP.
- Clot removal – proteced by the clot, the vessel wall is restored by new tissue formation.

  The clot is then removes, mainly by the proteolytic enzyme plasmin from plasmiogen activated by plasminogen actovators from λ granules.

Three dimension structure of blood clot



Blood clot cascade reaction



Bone Marrow

&

Hematopoiesis (Hemopoiesis)

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Bone Marrow

- Bone marrow, a gelatinous, vascular connective tissue located in the marrow cavity and constitutes almost 5% of the total body weight.
- Bone marrow is isolated from bone by the endosteum.
- It is responsible for the formation of blood cells (hemopoiesis) and their delivery into the circulatory system and start to perform the function from the fifth month of prenatal life until the person dies.
- Bone marrow also provides a microenvironment for much of the maturation process of B lymphocytes and for the initial maturation of T lymphocytes.

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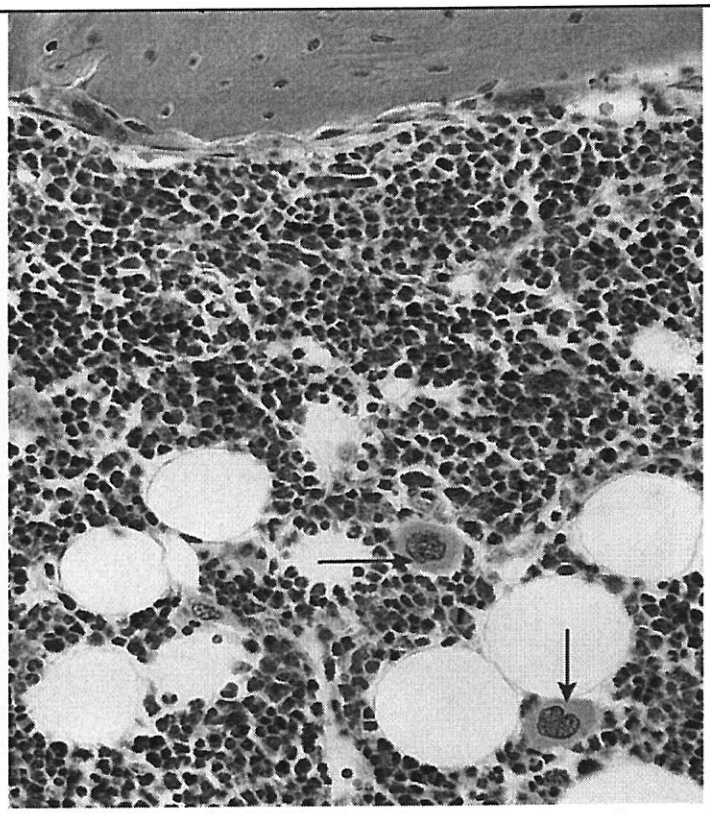
Bone Marrow



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Vascular supply to bone marrow

- The vascular supply of bone marrow is derived from the nutrient arteries that pierce the diaphysis via the nutrient foramina, tunnels leading from the outside surface of bone into the medullary cavity.
- These arteries enter the marrow cavity and give rise to a number of small, peripherally located vessels that provide numerous branches both centrally, to the marrow, and peripherally, to the cortical bone.
- Vessels entering the cortical bone are distributed through the haversian and Volkmann canals to serve the compact bone.

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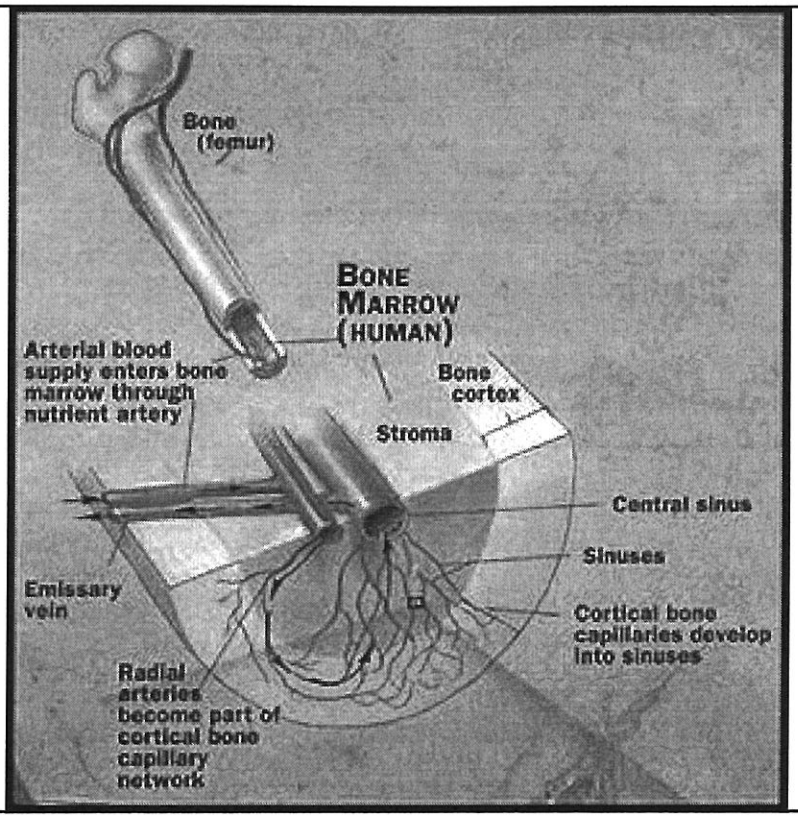

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- The centrally directed branches deliver their blood to the extensive network of large sinusoids (45 - 80 μm in diameter).
- The sinusoids drain into a central longitudinal vein, which is drained by veins leaving the bone via the nutrient canal.
- The veins are smaller than the arteries, thus establishing high hydrostatic pressure within the sinusoids, thus preventing their collapse.
- The veins, arteries, and sinusoids form the vascular compartment, and the intervening spaces are filled with pleomorphic islands of hemopoietic cells that merge with each other, forming the hemopoietic compartment.

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Two Types of Bone Marrow

- The marrow of the newborn is called red marrow because of the great number of erythrocytes being produced there.
- By age 20 years, however, the diaphyses of long bones house only yellow marrow because of the accumulation of large quantities of fat and the absence of hemopoiesis in the shafts of these bones.

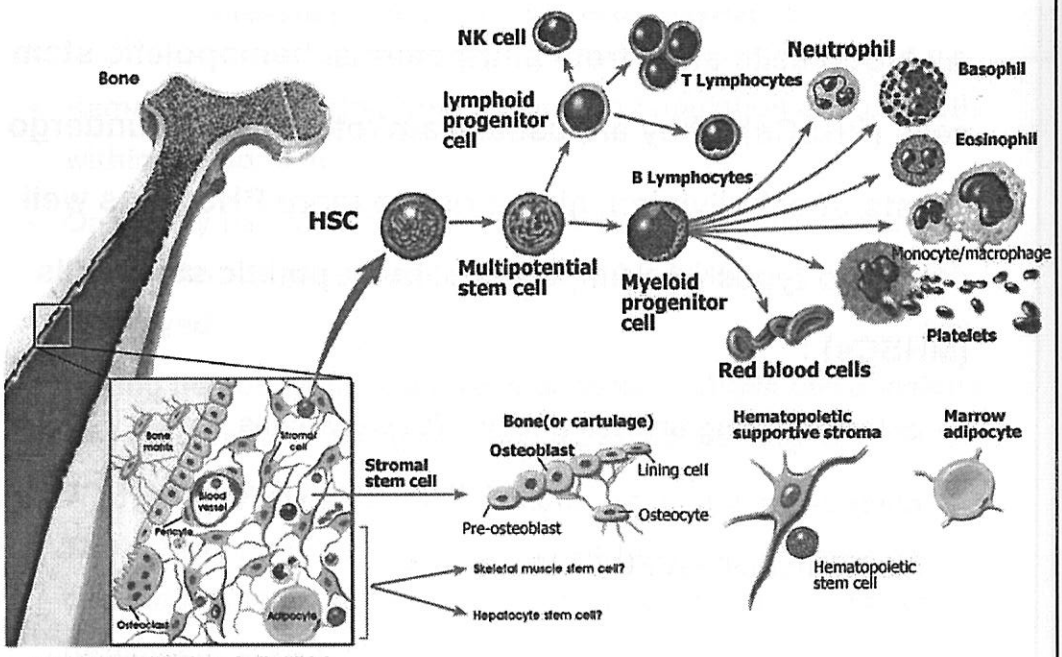
Hematopoiesis or Hemopoiesis

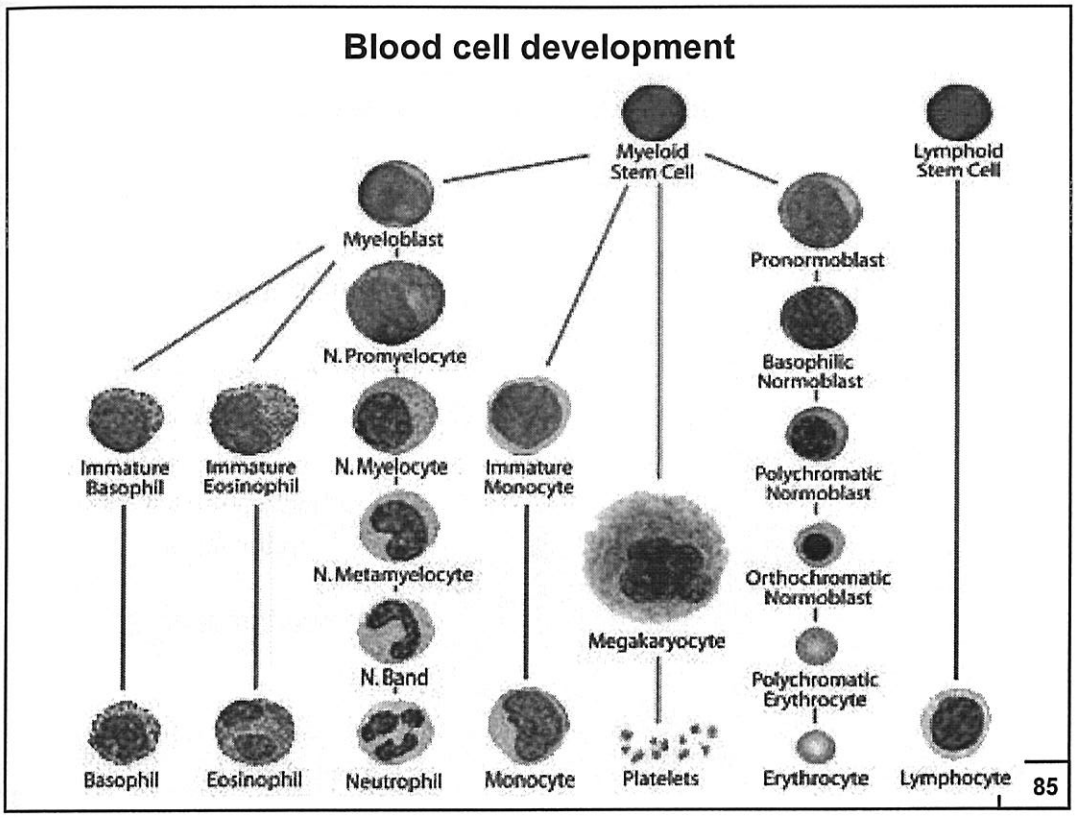
- Hemopoiesis, starting from a common population of stem cells within the bone marrow.
- On a daily basis, more than 10^{11} blood cells are produced in the marrow to replace cells that leave the bloodstream, die, or are destroyed.
- During hemopoiesis, stem cells undergo multiple cell divisions and differentiate through several intermediate stages, eventually giving rise to the mature blood cells.
- The entire process is regulated by various growth factors and cytokines that act at different steps to control the type of cells formed and their rate of formation.

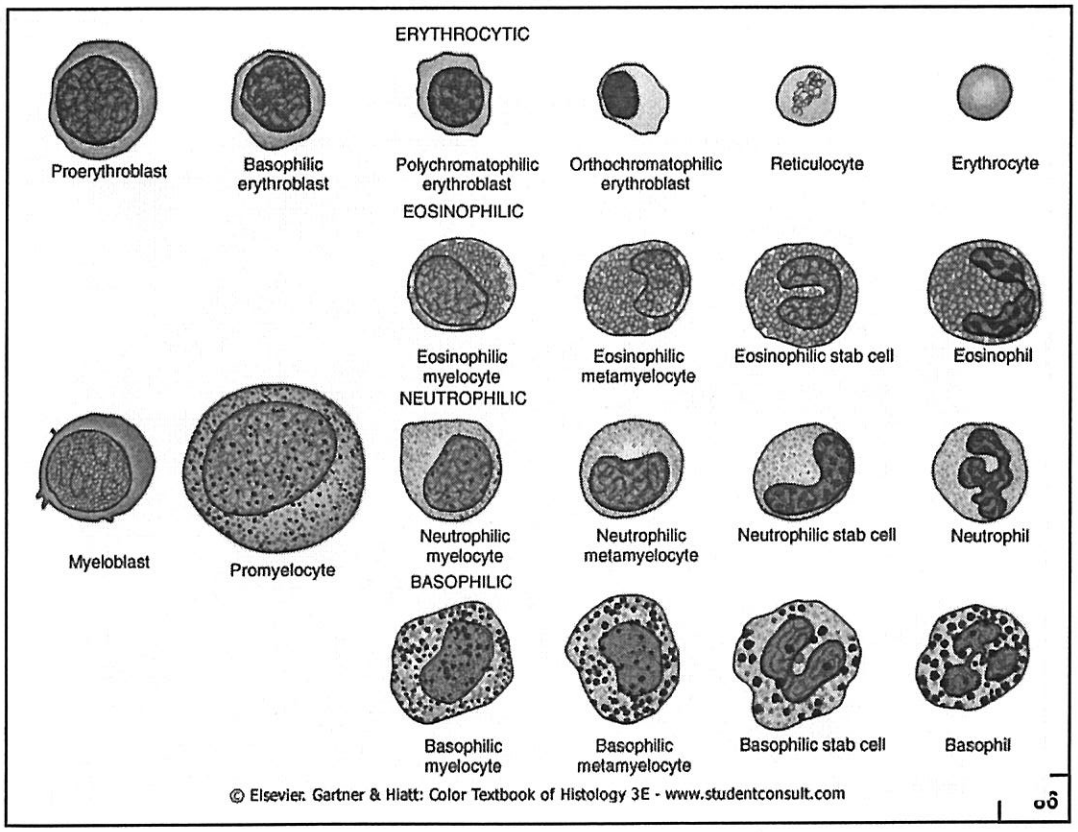
- Totipotency is the ability of a single cell to divide and produce all the differentiated cells in an organism, including extraembryonic tissues.
- Pluripotency in the broad sense refers to "having more than one potential outcome". In biological systems, this can refer either to cells or to biological compounds.
- Multipotent progeniotr cells can give rise to several other cell types, but those types are limited in number. An example of a multipotent stem cell is a hematopoietic cell — a blood stem cell that can develop into several types of blood cells, but cannot develop into brain cells or other types of cells.
- unipotent cell is one that has the capacity to develop/differentiate into only one type of tissue/cell type. The most common of these in humans are skin cells.

- All blood cells arise from pluripotential hemopoietic stem cells (PHSCs). They are usually amitotic but may undergo bursts of cell division, giving rise to more PHSCs as well as to two types of multipotential hemopoietic stem cells (MHSCs) :
  - colony-forming unit-lymphocyte (CFU-Ly) cells
  - colony-forming unit-granulocyte, erythrocyte, monocyte, megakaryocyte (CFU-GEMM) cells

- colony-forming unit-lymphocyte (CFU-Ly) cells
  - predecessors of the lymphoid cell lines
    - + T cells and
    - + B cells
- colony-forming unit-granulocyte, erythrocyte, monocyte, megakaryocyte (CFU-GEMM) cells
  - predecessors of the myeloid cell lines
    - + erythrocytes,
    - + granulocytes,
    - + monocytes, and
    - + platelets




Blood cell development
Myeloid Stem Cell
Lymphoid Stem Cell
Myeloblast
Promormoblast
N. Promyelocyte
Basophilic Normoblast
Immature Basophil
Immature Eosinophil
N. Myelocyte
Immature Monocyte
Polychromatic Normoblast
N. Metamyelocyte
Orthochromatic Normoblast
Megakaryocyte
N. Band
Polychromatic Erythrocyte
Basophil
Eosinophil
Neutrophil
Monocyte
Platelets
Erythrocyte
Lymphocyte
85


ERYTHROCYTIC
Proerythroblast
Basophilic erythroblast
Polychromatophilic erythroblast
Orthochromatophilic erythroblast
Reticulocyte
Erythrocyte
EOSINOPHILIC
Eosinophilic myelocyte
Eosinophilic metamyelocyte
Eosinophilic stab cell
Eosinophil
NEUTROPHILIC
Myeloblast
Promyelocyte
Neutrophilic myelocyte
Neutrophilic metamyelocyte
Neutrophilic stab cell
Neutrophil
BASOPHILIC
Basophilic myelocyte
Basophilic metamyelocyte
Basophilic stab cell
Basophil
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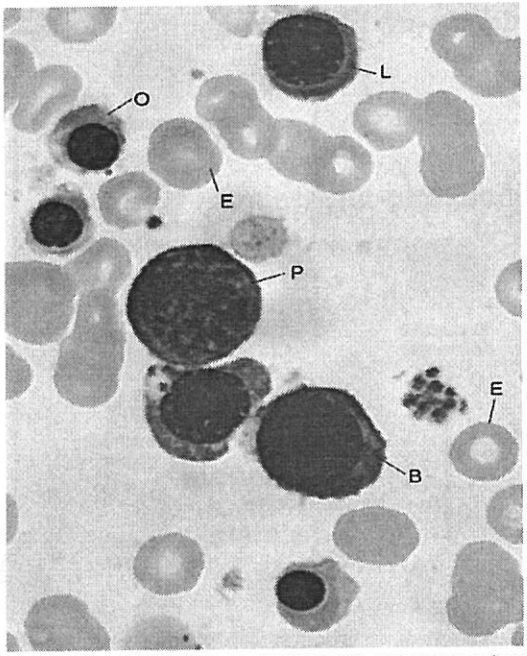
Erythropoiesis

(differentiation of erythrocyte)



B = basophilic erythroblast

E = erythrocyte

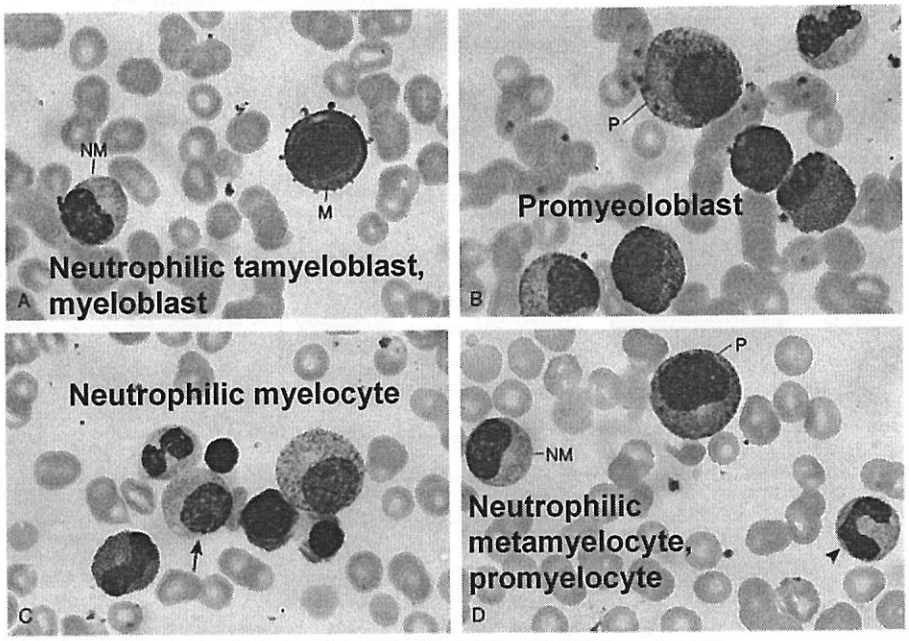
L = polychromatophilic erythroblast

O = orthochromatophilic erythroblast

P = proerythroblast

Granulopoiesis

(differentiation of neuttophil, basophil & eosinophil)



PowerPoint

เรื่อง

Lymphoreticular System

รองศาสตราจารย์ ดร. กรกช อินทราพิชฐ

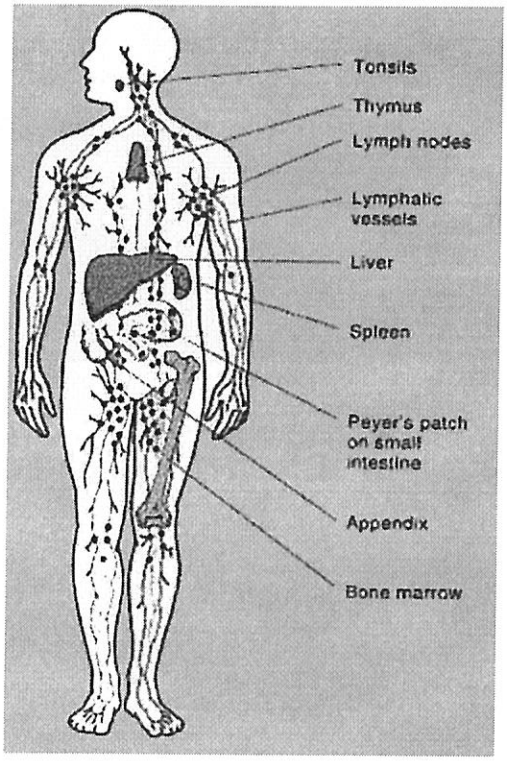
Lymphoreticular System

Blood- & Lymph-Forming Organs

Blood- & Lymph-Forming Organs

- **The lymphoid system is responsible for the immunological defense of the body.**
- **The cells of the lymphoid system protect the body against foreign macromolecules, viruses, bacteria, and other invasive microorganisms, and they kill virally transformed cells.**
- **Some of its component organs- lymph nodes, thymus, and spleen-are surrounded by connective tissue capsules, whereas its other components, members of the diffuse lymphoid system, are not encapsulated.**

Lympoid Organs



3

Types of Immune Responses

- The immune system has two components: the innate immune system and the adaptive immune system.
- The innate immune system :

  The first line of defense is the epithelial barrier, namely skin and mucosa, which forms a complete lining and covering of the body surfaces.
- The adaptive (acquired) immune system :

  The second lines of defenses against invading pathogens, become activated, once the physical barriers are breached by a cut, tear, or abrasion, or even if foreign substances are able to penetrate.

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Innate Immune System

- The innate immune system (natural immune system) is nonspecific, rapid manner and has no immunological memory; and is composed of

(1) a system of blood-borne macromolecules known as complement (proteins found in the blood, which work together to kill target cells by disrupting the target cell's plasma membrane);

(2) groups of cells known as macrophages and neutrophils, which phagocytose invaders; and

(3) another group of cells, natural killer (NK) cells, which kill tumor cells, virally infected cells, bacteria, and parasites.

- The critical components of the innate immune system are
  - complement,
  - antimicrobial peptides,
  - cytokines,
  - macrophages,
  - neutrophils,
  - NK cells, and
  - Toll-like receptors (TLRs).

Adaptive (Acquired) Immune System

- The adaptive immune system (acquired immune system) is responsible for eliminating threats from specific invaders.
- Whereas a macrophage can phagocytose most bacteria, the adaptive immune system not only reacts against one specific antigenic component of a pathogen, but also its ability to react against that particular component improves with subsequent confrontations with it.
- The adaptive immune system responds slower than the innate immune system, has immunological memory, and depends on B and T lymphocytes to mount an immune response.

Lymphoid organs

The lymphoid organs are classified into two categories:

1 Primary (central) lymphoid organs are responsible for the development and maturation of lymphocytes into mature, immunocompetent cells. They are bone marrow & thymus.

2 Secondary (peripheral) lymphoid organs are responsible for the proper environment in which immunocompetent cells can react with each other, as well as with antigens and other cells, to mount an immunological challenge against invading antigens or pathogens. They are diffuse lymphoid tissue, lymph nodes, and Spleen

Lymphoid Tissue

- Lymphoid tissue is a type of CT characterized by
  - rich supply of lymphocytes,
  - free cells within capsules forming lymphoid organs
  - rich network of reticular fibrils that supports the cells.
- The reticular fibrils are produced by a fibroblast cell called a reticular cell, except thymus.

Three types of lymphoid tissues

1. Loose lymphoid tissue: The network has fewer but larger spaces for cells freely to move.
2. Dense lymphoid tissue: The network of reticular fibrils is relatively close so that it is able to hold many free cells, macrophages, and plasma cells.
3. Nodular lymphoid tissue or lymphatic nodule or lymphatic follicle: typical spherical structures surrounded by diffuse tissue, found in all of lymphatic organ (except thymus), and in loose CT of several organs, mainly in the lamina propria of GI tract such as Peyer's patches in the ileum.

Lymphoid Nodules

Two types of lymphoid nodules:

Primary and secondary &

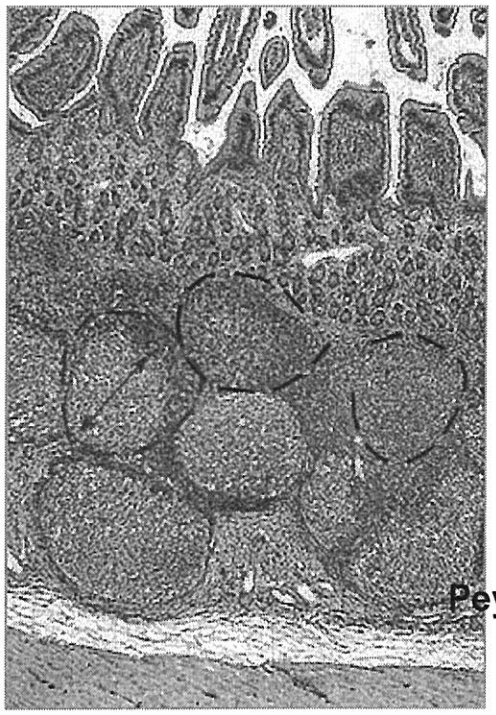
Secondary lymphoid nodules with a germinal center

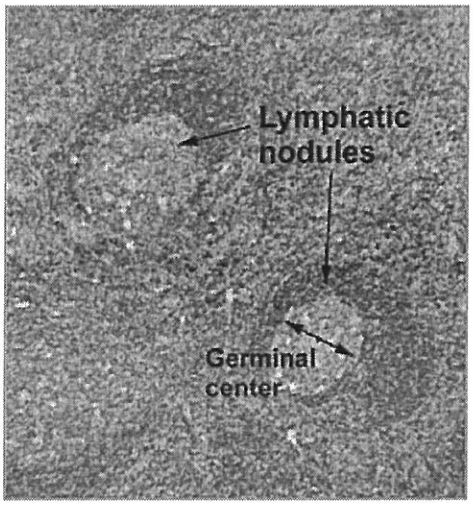
Lymphoid (lymphatic) Nodules

- **Lymphoid nodules are lymphoid structures common along the gastrointestinal tract**
- **The highest development of lymphoid nodules are in the appendix and ileum**modular lymphatic tissue
- **Lymphoid nodules and lymphocytic infiltrations commonly occur together in the lamina propria and many areas.**

Two types of lymphoid nodules

- Primary nodule appears as a homogenous mass of lymphocytes or
- Secondary nodule with a germinal center containing large pale cells surrounded by a dense cortex of small lymphocytes.
- Peyer's patches - both solitary nodules and the larger and more extensive aggregated nodules.





Peyer's pathces

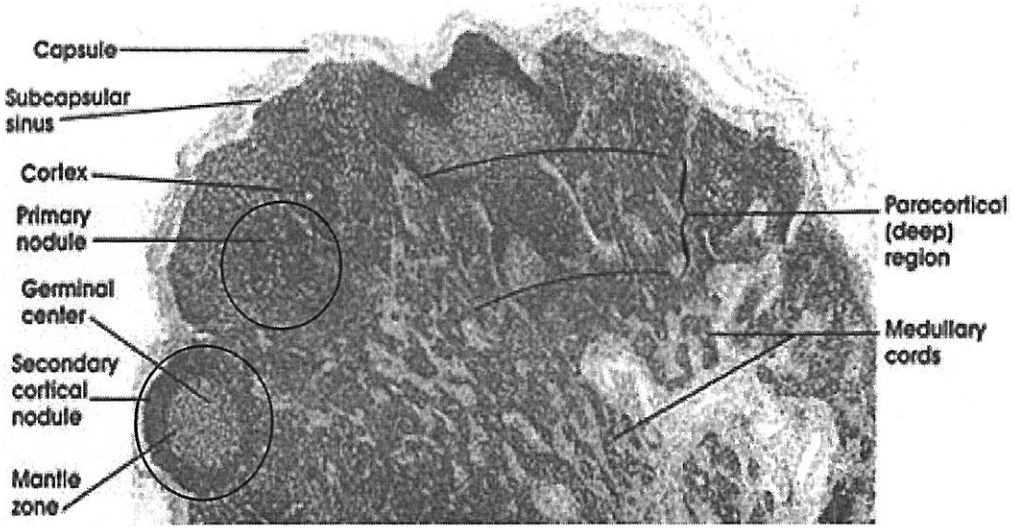
Primary lymphoid nodules

- Primary lymphoid nodules are spherical aggregates of B lymphocytes (both virgin B cells and B memory cells) that are in the process of entering or leaving the lymph node.
- Primary lymphoid nodules have incomplete compartments within the cortex.

Secondary lymphoid nodules

- The centers of the secondary lymphoid nodules are stained pale, called germinal centers.
- Secondary lymphoid nodules form only in response to an antigenic challenge; it is believed that they are the sites of B memory cell and plasma cell generation.
- The region of the lymphoid nodule peripheral to the germinal center is composed of a dense accumulation of small lymphocytes that are migrating away from their site of origin within the germinal center. This peripheral region is called the corona (mantle).

1° & 2° Lymphatic nodules in lymph node



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Germinal centers

- Germinal centers display three zones: a dark zone, a basal light zone, and an apical light zone.

1. The dark zone is the site of the intense proliferation of closely packed B cells. These cells, know as centroblasts, migrate into
2. The basal light zone, express Igs, switch immunoglobulin class, and are known as centrocytes. These cells are exposed to antigen-bearing follicular dendritic cells and undergo somatic hypermutation of genes to become more proficient at forming antibodies against the antigen.
3. The apical light zone, where The newly formed centrocytes that are permitted to enter and become either B memory cells or plasma cells and subsequently leave the secondary follicle.

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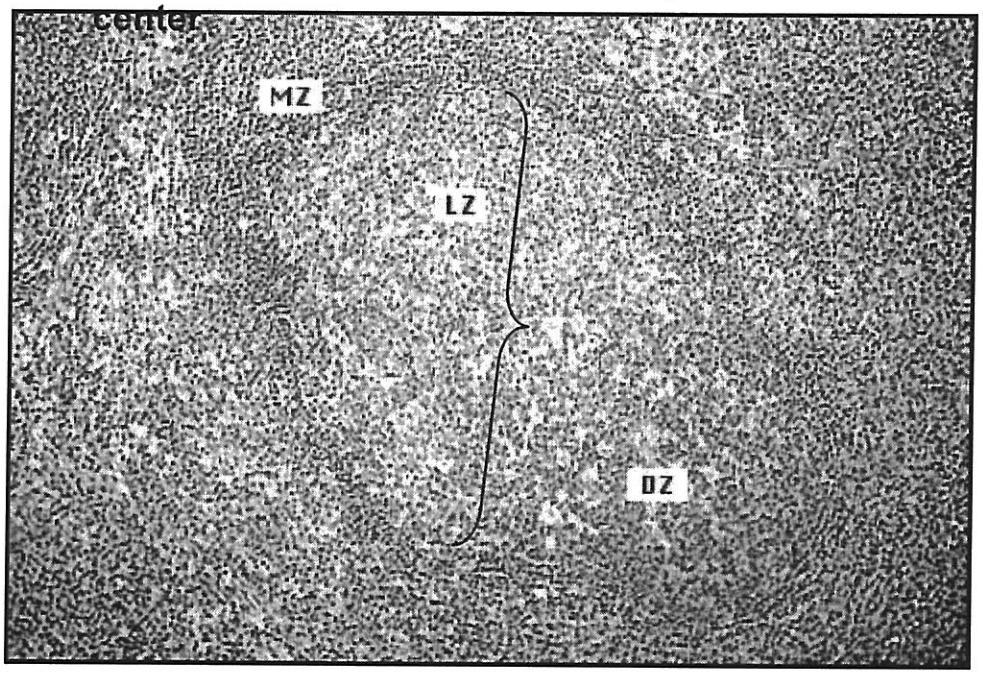
Secondary Lypmoid Nodule with germinal center



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Mucosa-Associated Lymphoid Tissue

- Mucosa-associated lymphoid tissue (MALT) is composed of a nonencapsulated, localized lymphocyte infiltration and lymphoid nodules in the mucosa of the gastrointestinal, respiratory, and urinary tracts.
  - gut-associated lymphoid tissue (GALT),
  - bronchus-associated lymphatic tissue (BALT), and the
  - tonsils.

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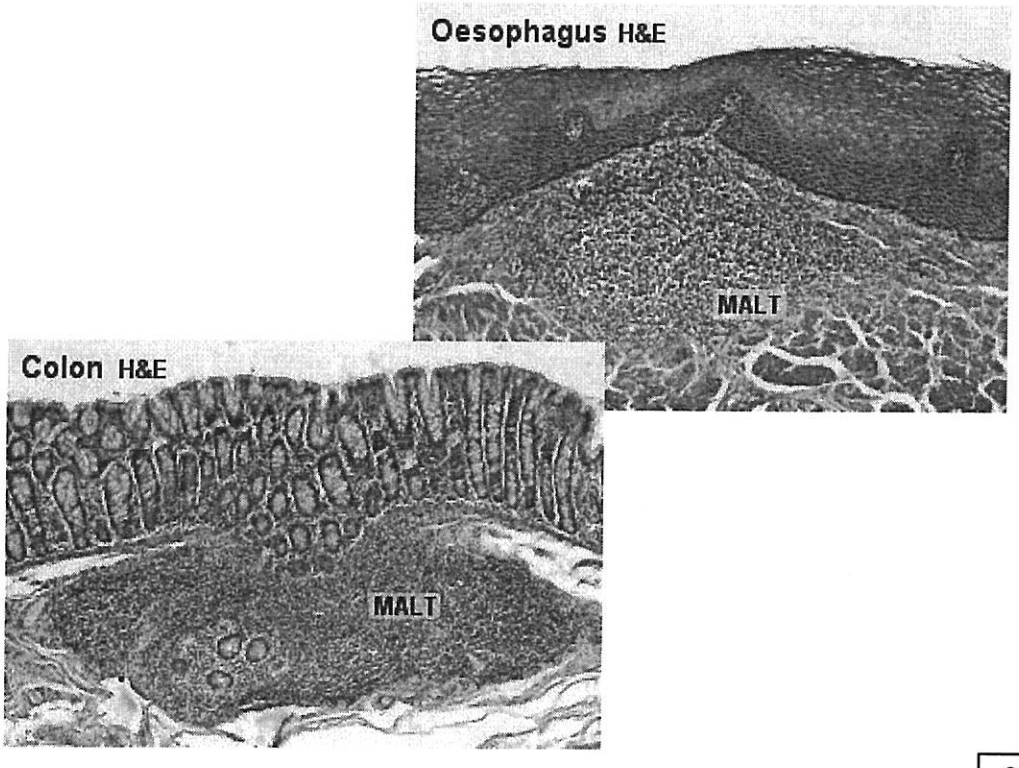
Gut-Associated Lymphoid Tissue (GALT)

- The most prominent of GALT is located in the ileum and is known as Peyer's patches.
- The Peyer's patches are composed of B cells surrounded by a looser region of T cells and numerous APCs.
- They are lined by squamous-like cells, known as microfold cells or M Cells for capturing antigens and transfering them to macrophages.
- They have no afferent lymphatic vessels, but they do have efferent lymph drainage. They receive small arterioles that form a capillary bed, drained by High Endothelial Venules (HEVs).

21



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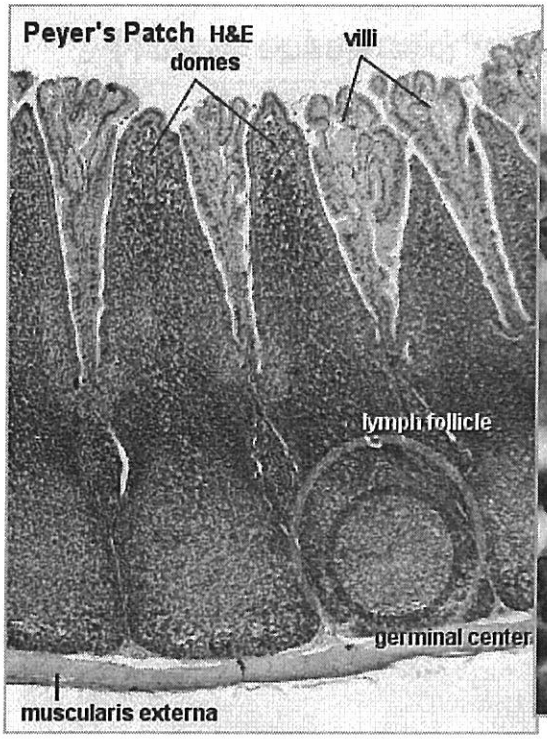

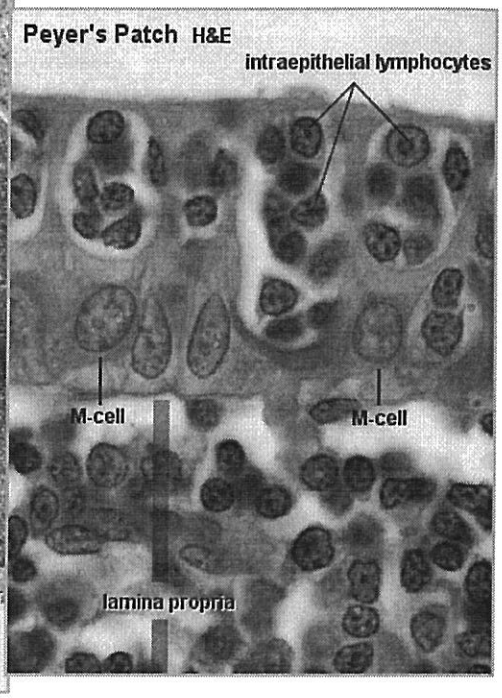

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Bronchus-Associated Lymphoid Tissue (BALT)

- BALT is similar to Peyer's patches, except that it is located in the walls of bronchi.
- The epithelial cover over these lymphoid nodules changes from a pseudostratified ciliated columnar with goblet cells to M cells.
- Afferent lymph vessels are absent, although lymph drainage has been demonstrated. The rich vascular supply of BALT indicates its possible systemic as well as localized role in the immune process.

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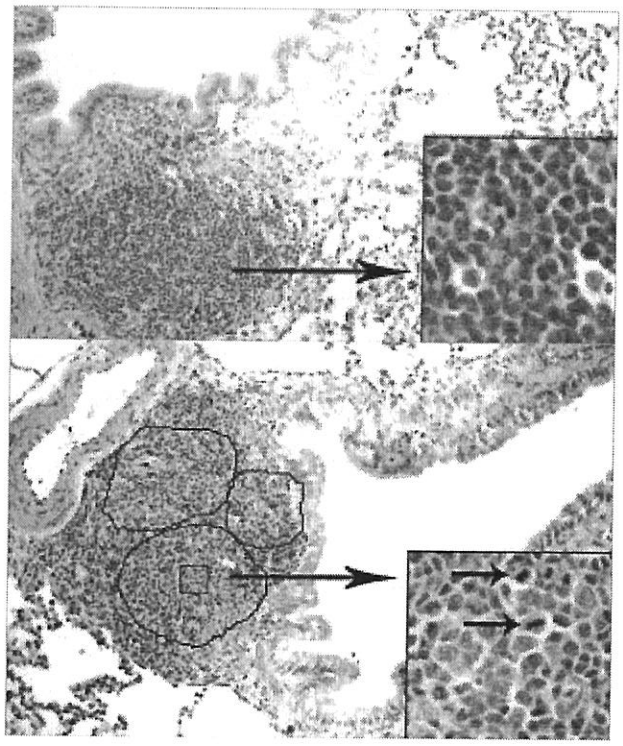
Bronchus-associated lymphoid tissue (BALT)



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Tonsils

- The tonsils are incompletely encapsulated aggregates of lymphoid nodules that guard the entrance to the oral pharynx.
- Tonsils are interposed into the path of airborne and ingested antigens.
- They react to these antigens by forming lymphocytes and mounting an immune response.
- There three tonsils named depending on locations;
  - Palatine
  - pharyngeal, and
  - lingual

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Palatine tonsils

- The bilateral palatine tonsils are located at the boundary of the oral cavity and the oral pharynx.
- Each palatine tonsil is isolated from the surrounding connective tissue by a dense, fibrous capsule and is covered by a stratified squamous nonkeratinized epithelium
- The epithelium dips into the 10 to 12 deep crypts that invaginate the tonsilar parenchyma.
- The parenchyma of the tonsil is composed of numerous lymphoid nodules, many of which display germinal centers, indicative of B-cell formation.

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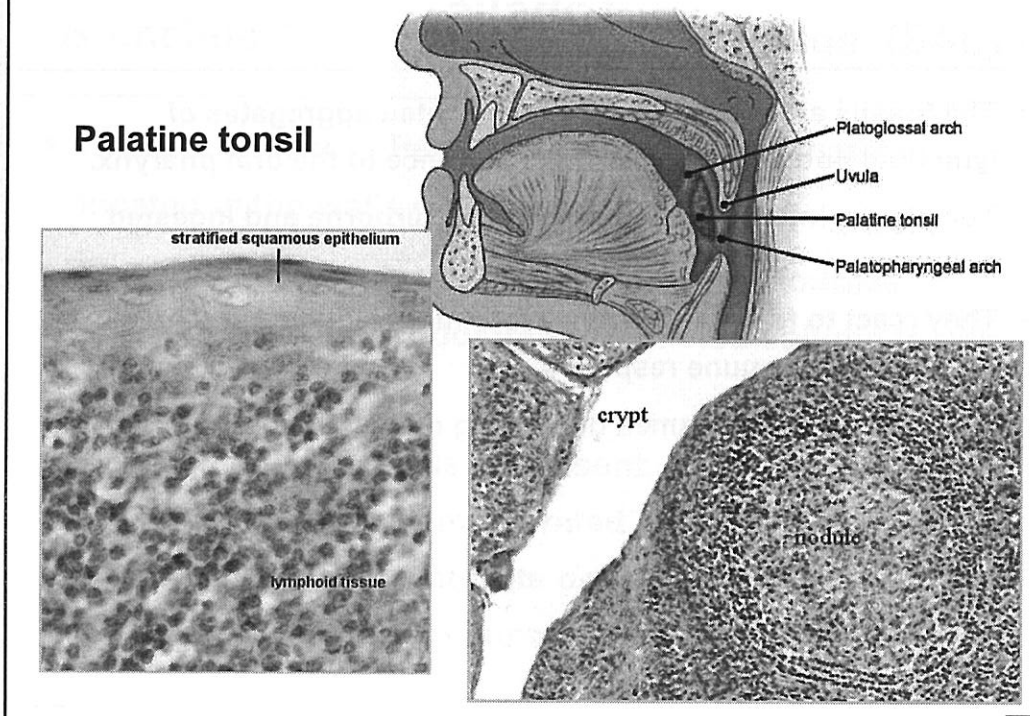

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Pharyngeal tonsil

- The single pharyngeal tonsil is in the roof of the nasal pharynx. It is similar to the palatine tonsils, but its incomplete capsule is thinner.
- The crypts, the pharyngeal tonsil has shallow, longitudinal infoldings called pleats.
- Its superficial surface is covered by a pseudostratified ciliated columnar epithelium that is interspersed with patches of stratified squamous epithelium.
- The parenchyma of the pharyngeal tonsil is composed of lymphoid nodules, some of which have germinal centers.
- When this type of tonsil is inflamed, it is called the adenoid.

Pharyngeal tonsil

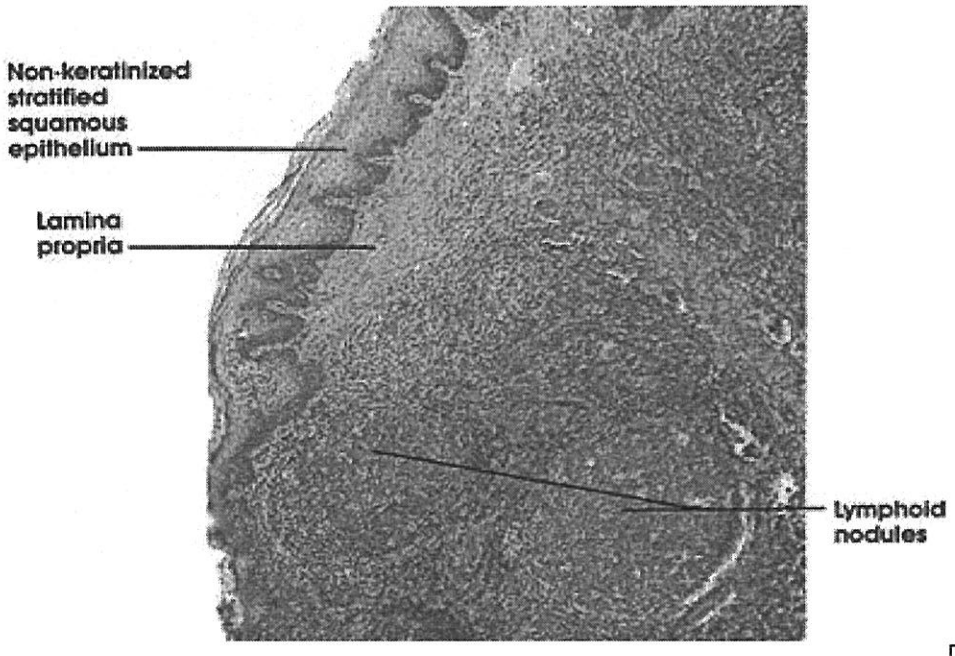
Lingual tonsil

- The lingual tonsil is located on the dorsal surface of the posterior one third of the tongue and is covered, on its superficial aspect, by a stratified squamous nonkeratinized epithelium.
- The deep aspect of the lingual tonsil has a flimsy capsule that separates it from the underlying connective tissue.
- The tonsil has numerous crypts, whose bases receive the ducts of mucous minor salivary glands.
- The parenchyma of the lingual tonsil is composed of lymphoid nodules, which frequently have germinal centers.

lingual tonsil

31

Lingual tonsil



32

Lymph Nodes

Lymph nodes are encapsulated and interposed in the path of lymph vessels.

The Lymph Filter

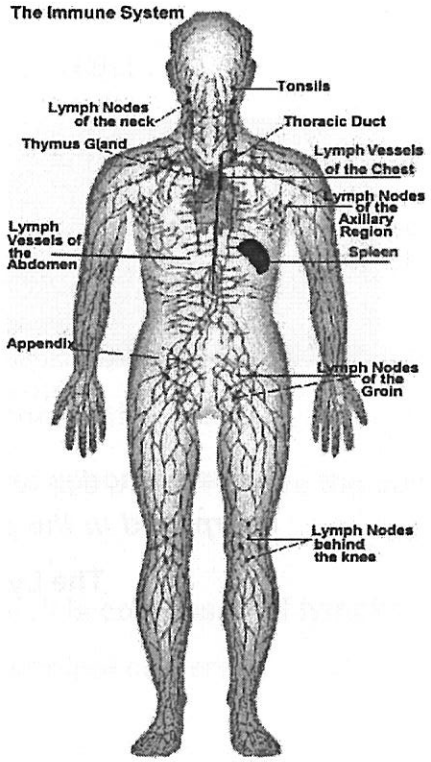
Lymph Nodes

- **Lymph nodes are covered with capsule, oval structures, and interposed in the path of lymph vessels to serve as filters for the removal of bacteria and other foreign substances from lymph.**
- **Lymph nodes occur along the entire length of the lymphatic system.**
- **They are most abundunt in the neck, in the axilla, in the groin, along major vessels, and in the body cavities.**
- **Their parenchyma is composed of collections of T and B lymphocytes, APCs, and macrophages.**
- **Macrophages in lymph nodes phagocytose bacteria and other microorganisms that enter the lymph node by way of the lymph.**

Lymph nodes

&

Lymphoid tissues



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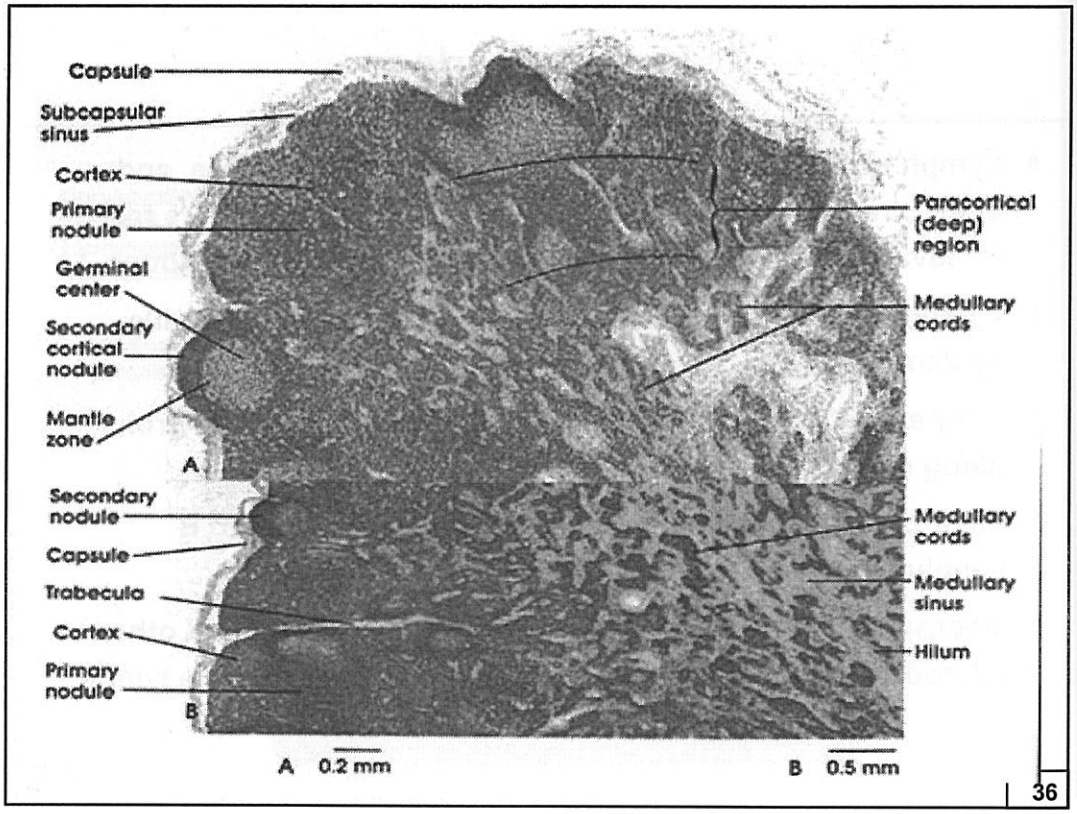

36

- lymph node is a relatively small, soft structure that is less than 3 cm in diameter and that has a fibrous connective tissue capsule, usually surrounded by adipose tissue.
- It has a convex surface that is perforated by afferent lymph vessels that have valves, which ensure that lymph from those vessels enters the substance of the node.
- The concave surface of the node, the hilum, is the site of arteries and veins entering and exiting the node.
- Lymph leaves the node via the efferent lymph vessels with valves, which are also located at the hilum.
- A lymph node is subdivided into two regions: cortex, and medulla. All three regions have a rich supply of sinusoids, enlarged endothelium-lined spaces through which lymph percolates.

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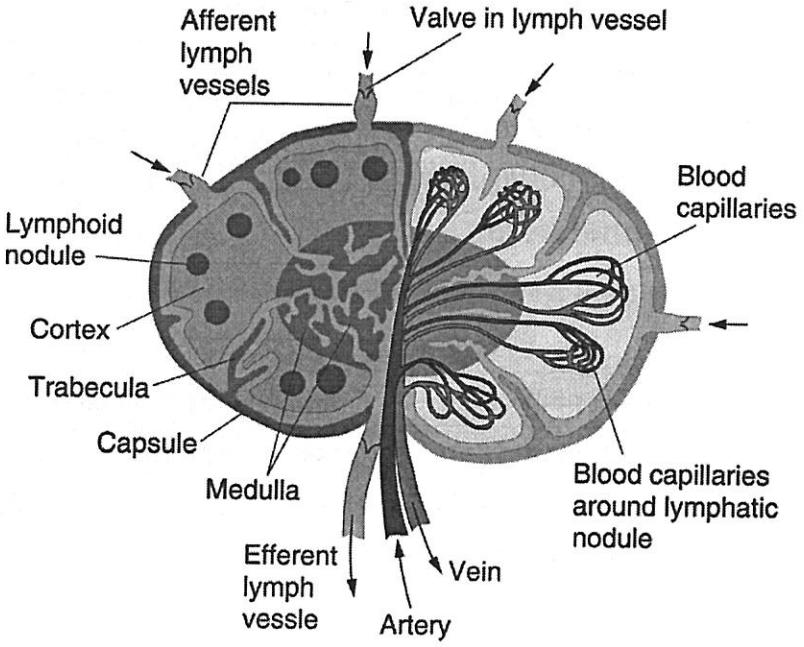
Lymph node & Blood circulation in lymph node



38

Lymph Node Cortex

- Capsule is connective tissue that sends trabeculae into the substance of the lymph node, subdividing the outer region of the cortex into incomplete compartments.
- The cortex can be subdivided into an outer and inner cortex or paracortical region.
- The cortex is composed of lymphoid nodules with germinal center and sinuses.

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Lymph Node Medulla

- The medulla has two components:

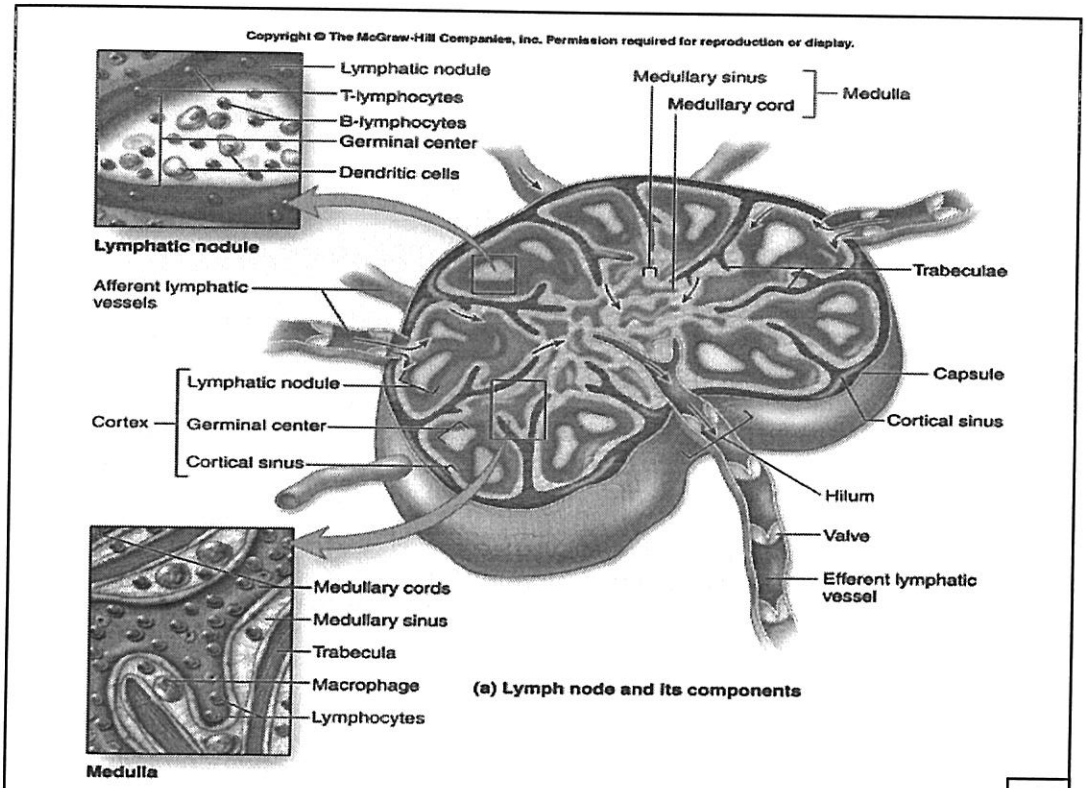
The medullary cords are branched cordlike extensions of dense lympoid tissue that arise in the inner cortex.

- They contain primary B lymphocytes and often plasma cells and macrophages.

The medullary sinuses are dilated spaces those separate the medullary cords, bridged by reticular cells and fiber, They contain lymph and lymphocytes.

- These sinuses join at the hilum delivering the lymph to the efferent lymph vessels of the lymph node.

40



41

Lymph circulation

- The afferent lymph vessels pierce the capsule on the convex surface of the node and empty their lymph into the subcapsular sinus and is continuous with the cortical sinuses (paratrabecular sinuses) that parallel the trabeculae and deliver the lymph into the medullary sinuses, eventually to enter the efferent lymphatic vessels.

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Thymus

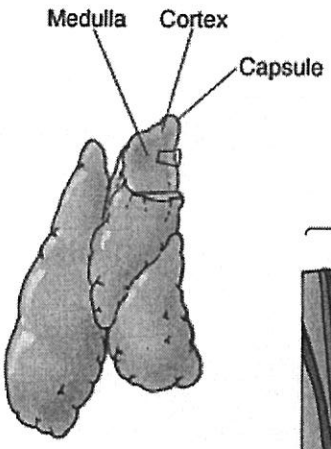
The thymus is a primary lymphoid organ that is the site of maturation of T lymphocytes.

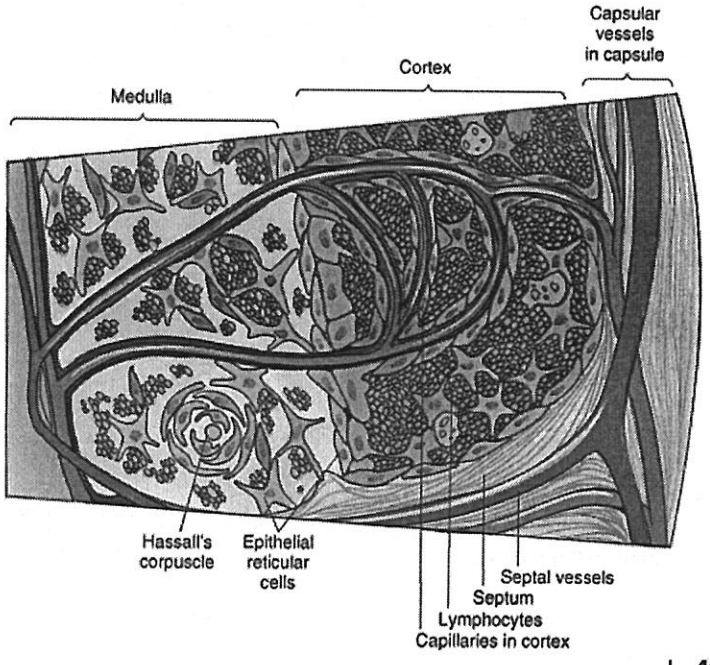
Thymus

- **The thymus, situated in the superior mediastinum and extending over the great vessels of the heart, is a small encapsulated organ composed of two lobes.**
- **The thymus originates early in the embryo and continues to grow until puberty, weigh as much as 35 to 40 g.**
- **After the first few years of life, the thymus begins to involute (atrophy) and becomes infiltrated by adipose cells.**
- **However, it may continue to function even in older adults.**

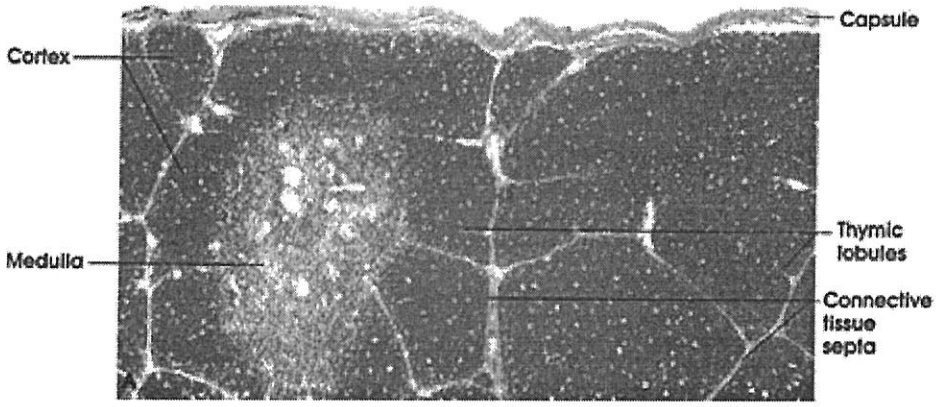
Thymic structure

- The capsule of the thymus, composed of dense, irregular collagenous connective tissue, sends septa into the lobes, subdividing them into incomplete lobules.
- Each lobule is composed of
  - cortex and
  - medulla, although the medullae of adjacent lobules are confluent with each other.





Thymic Histology

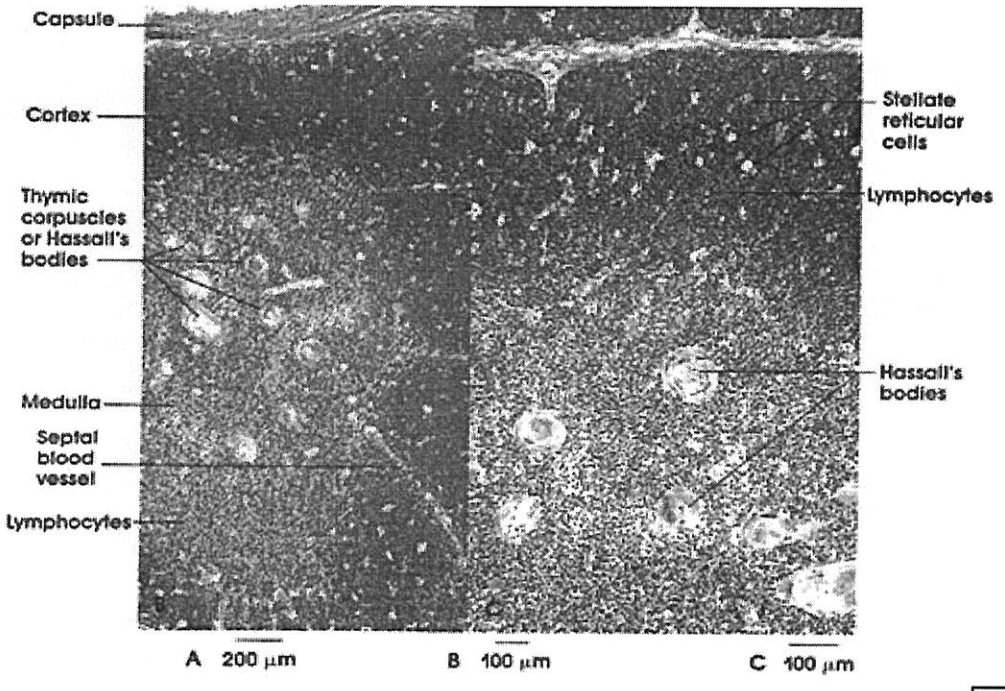


Thymic Cortex

- The cortex of the thymus appears much darker histologically than does the medulla because of the presence of a large population of T lymphocytes (thymocytes)
- Immunologically incompetent T cells leave the bone marrow and migrate to the periphery of the thymic cortex, where they undergo extensive proliferation and instruction to become immunocompetent T cells.
- In addition to the lymphocytes, the cortex houses macrophages and epithelial reticular cells.

- Epithelial reticular cells completely isolate the thymic cortex and thus prevent developing T cells from contacting foreign antigens.
- T cells die in the cortex and are phagocytosed by resident macrophages, which are referred to as tingible body macrophages.
- The surviving cells enter the medulla of the thymus as naïve T lymphocytes, and from there (or from the corticomedullary junction) they are distributed to secondary lymphoid organs via the vascular system.

Thymic cortex & medulla



Thymic Medulla

- The medulla is characterized by the presence of Hassall's corpuscles.
- All thymocytes of the medulla are immunocompetent T cells.
- The thymic medulla stains much lighter than the cortex because its lymphocyte population is not nearly as profuse and because it houses a large number of endothelially derived epithelial reticular cells.
- Epithelial reticular cells form whorl-shaped thymic corpuscles (Hassall's corpuscles), whose numbers increase with a person's age.

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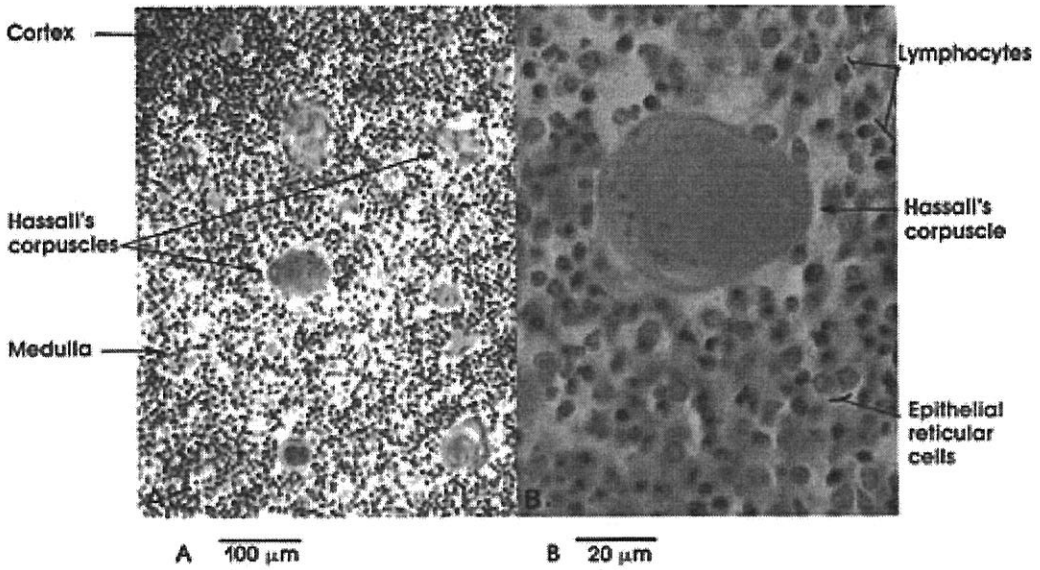
Hassall's corpuscle



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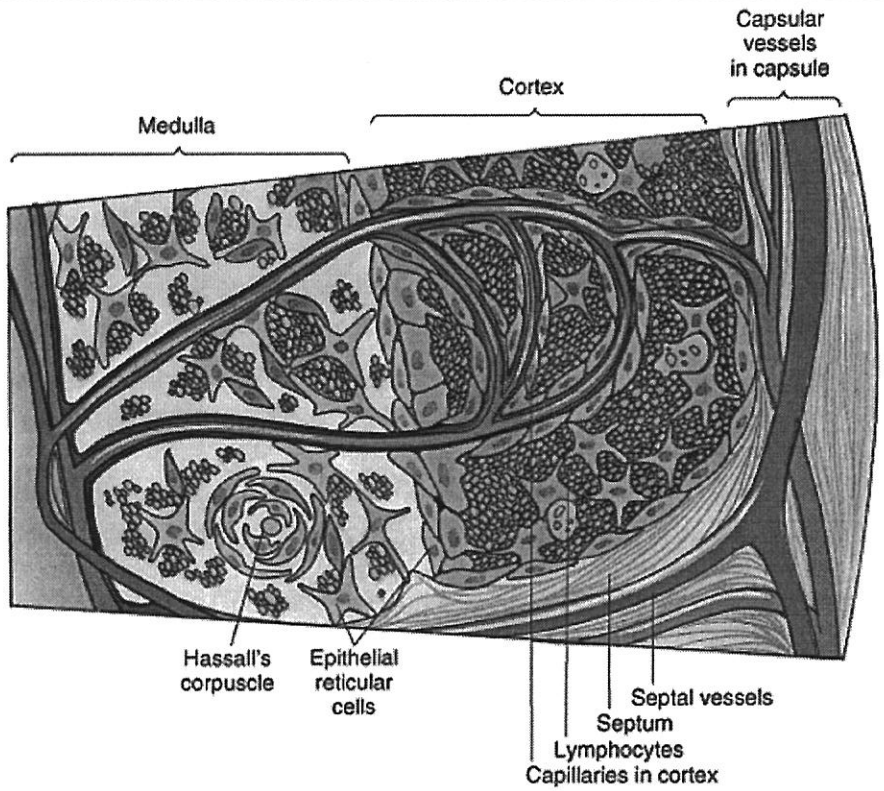
Vascular Supply to Thymus

- The cortical vascular supply forms a very powerful blood-thymus barrier to prevent developing T cells from contacting blood-borne macromolecules.
- The thymus receives numerous small arteries, which enter the capsule and are distributed throughout the organ via the trabeculae between adjacent lobules.
- Branches of these vessels do not gain access to the cortex directly; instead, from the trabeculae they enter the corticomedullary junction, where they form capillary beds that penetrate the cortex.

- The capillaries of the cortex and a sheath of epithelial reticular cells form a blood-thymus barrier, protecting developing T cells of the cortex from contacting blood-borne macromolecules.
- However, self-macromolecules are permitted to cross the blood-thymus barrier possibly to eliminate those T cells that are programmed against self-antigens.
- The cortical capillary network drains into small venules in the medulla.



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Function of Thymus

- The primary function of the thymus is to instruct immunoincompetent T cells to achieve immunocompetence.
- The developing T cells proliferate extensively in the cortex, begin to express their surface markers, and are tested for their ability to recognize self-MHC molecules and self-epitopes.
- T cells that are unable to recognize self-MHC I and self-MHC II molecules are destroyed by being driven into apoptosis.

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- The epithelial reticular cells of the thymus produce at least four hormones that are necessary for the maturation of T cells. These are probably paracrine hormones, acting at short range, although some are believed to be released into the bloodstream.
- These hormones facilitate T-cell proliferation and the expression of their surface markers;
  - thymosin,
  - thymopoietin,
  - thymulin, and
  - thymic humoral factor

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Spleen

The largest lymphoid organ in the body

The Blood Filter

58

Spleen

- The spleen is the largest accumulation of the lymphoid tissue in the body and the only one interposed in the blood circulation.
- The spleen is located in the peritoneum in the upper left quadrant of the abdominal cavity.
- Its dense, irregular fibroelastic connective tissue capsule, occasionally housing smooth muscle cells, is surrounded by visceral peritoneum.
- The simple squamous epithelium of the peritoneum provides a smooth surface for the spleen.

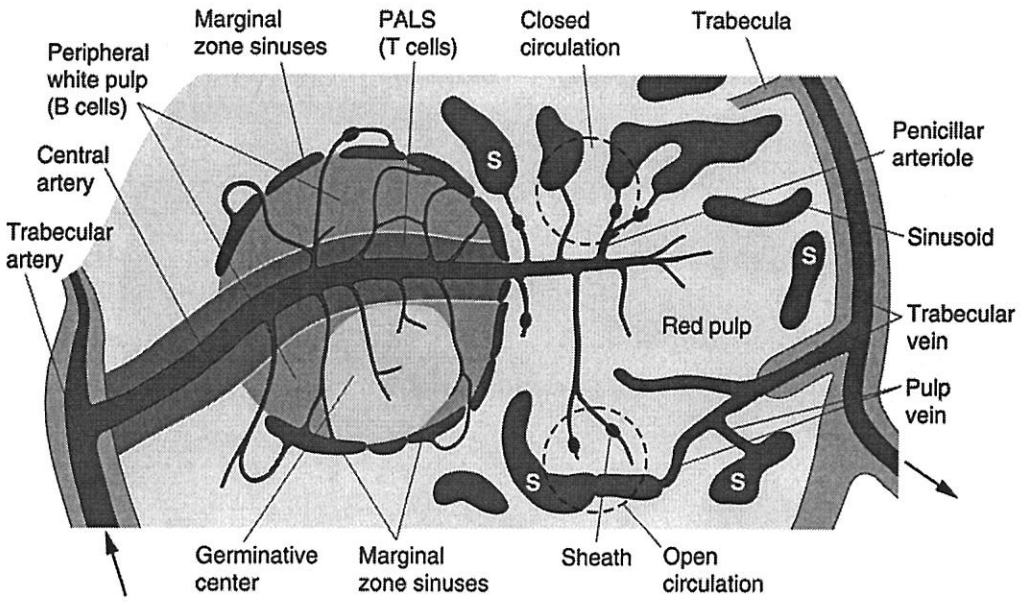
Splenic Structure

- The spleen has a convex surface and a concave aspect known as the hilum where is the entry and leave of
  - arteries
  - nerve
  - veins
  - lymph vessels
- The spleen is surrounded by a capsule of dense CT from which emerge trabeculae.
- The trabeculae divide the parenchyme or plenic pulp in to incomplete compartments.
- The trabeculae carry nerve, arteries and veins.
- Lymphatic vessels arise in the splenic pulp and leave the trabeculae to the hilum.

Vascular supply of the spleen

- The splenic artery and the splenic vein enter and leave the spleen at the hilum.
- The splenic artery branches repeatedly and pierces the connective tissue capsule at the hilum.
- Branches of these vessels, trabecular arteries, are conveyed into the spleen by trabeculae of decreasing sizes.
- The tunica adventitia of these vessels that left the trabeculae become loosely organized, called the central artery.
- The cenral artery is infiltrated by a sheath of T lymphocytes, called the periarterial lymphatic sheath (PALS).

Vascular supply of spleen



- The central artery loses its lymphatic sheath (PALS) and subdivides into several short, parallel branches, known as penicillar arteries, which enter the red pulp.
- The penicillar arteries have three regions:
  (1) the pulp arteriole,
  (2) the sheathed arteriole (a thickened region of the vessel surrounded by a sheath of macrophages termed the Schweigger-Seidel sheath), and
  (3) the terminal arterial capillaries.

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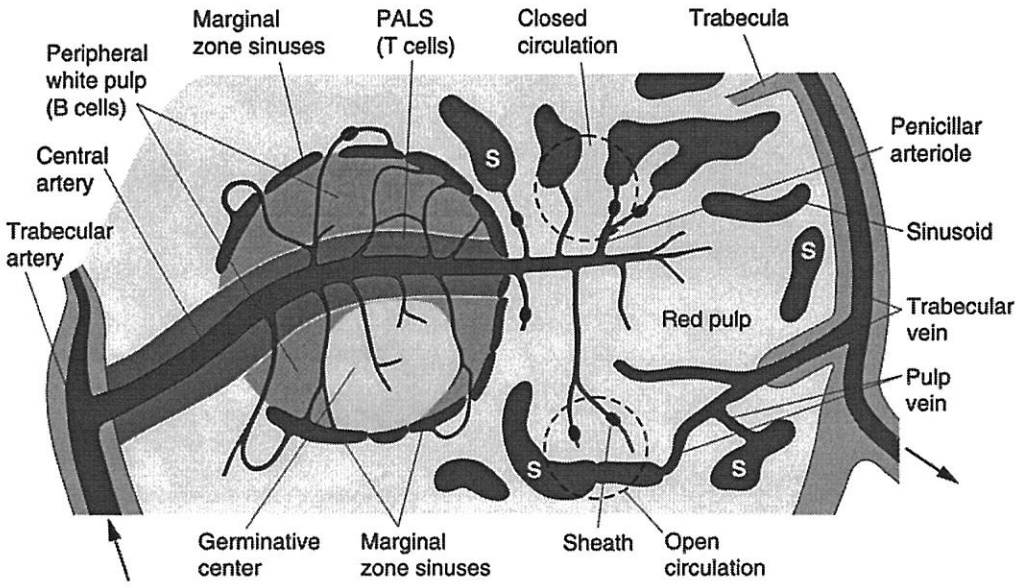
Vascular supply of spleen



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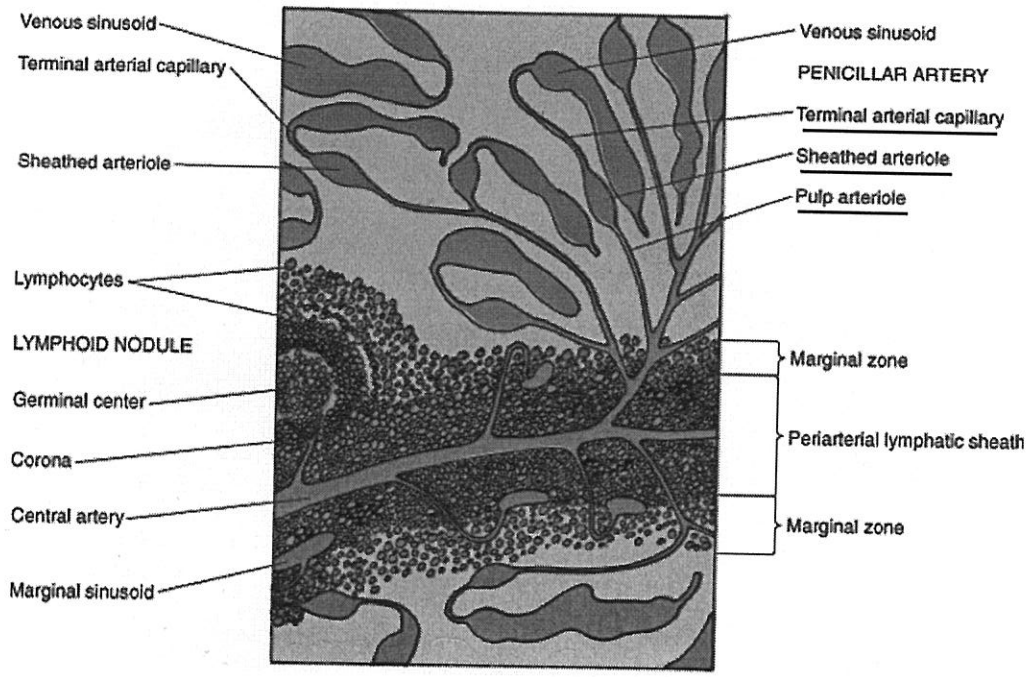

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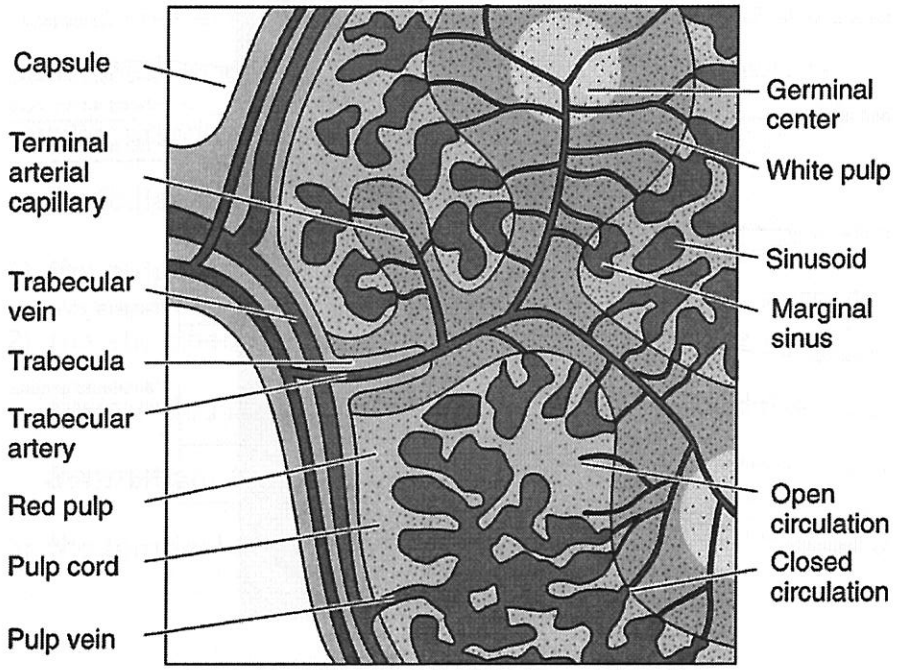
- The terminal arterial capillaries deliver their blood into the splenic sinuses by three theories of spleen circulation:
  (1) closed circulation,
  (2) open circulation, and
  (3) a combination of the first two theories.

- Splenic sinuses are drained by small veins of the pulp, which are tributaries of larger and larger veins that merge to form the splenic vein, a tributary of the portal vein.

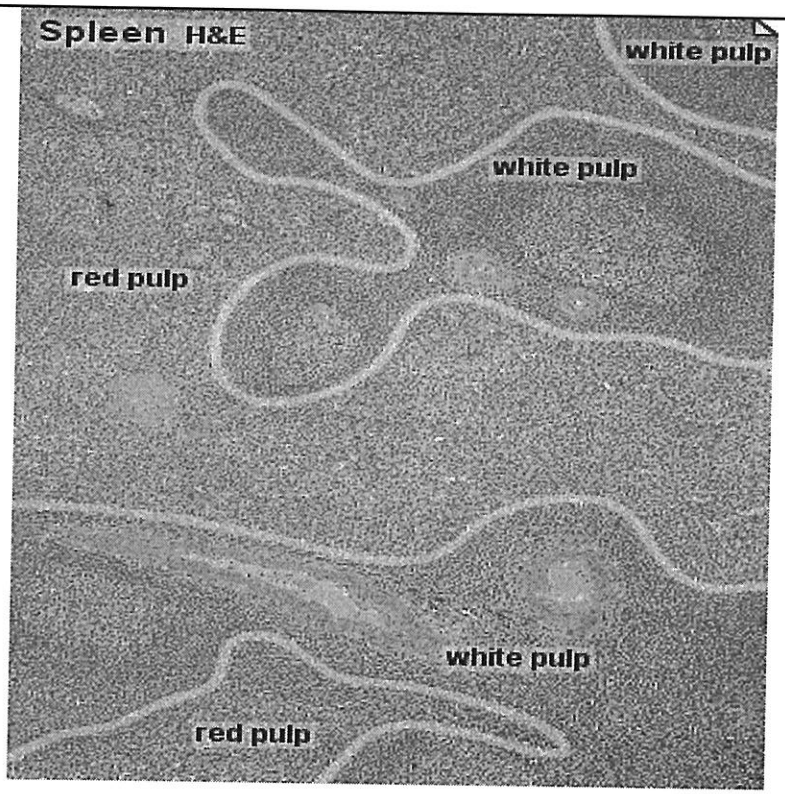
66

Capillary termination in spleen



Splenic Pulps

- **The splenic pulp has two components;**
  - **White pulp consists of periarterial lymphatic sheath (PALS)**
  - **Red pulp consists of splenic cords (Billroth's cord) and blood sinusoids.**



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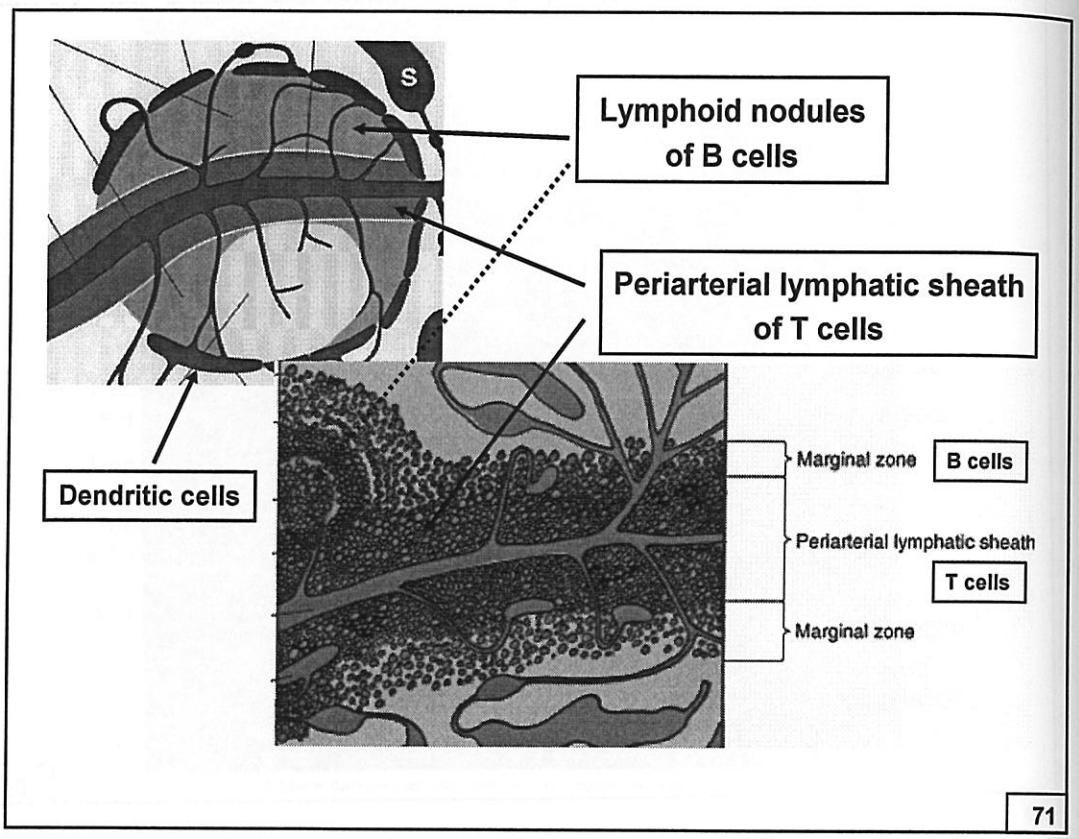
White Pulp and Marginal Zone

- The white pulp is composed of the periarterial lymphatic sheath of T cells, and lymphoid nodules of B cells.
- The marginal zone of B cells that are specialized to recognize thymic-independent antigens.
- The structure of the white pulp is closely associated with the central arteriole.
- The PALS is composed of B cells that surrounds the central arteriole is composed of T cells.

70



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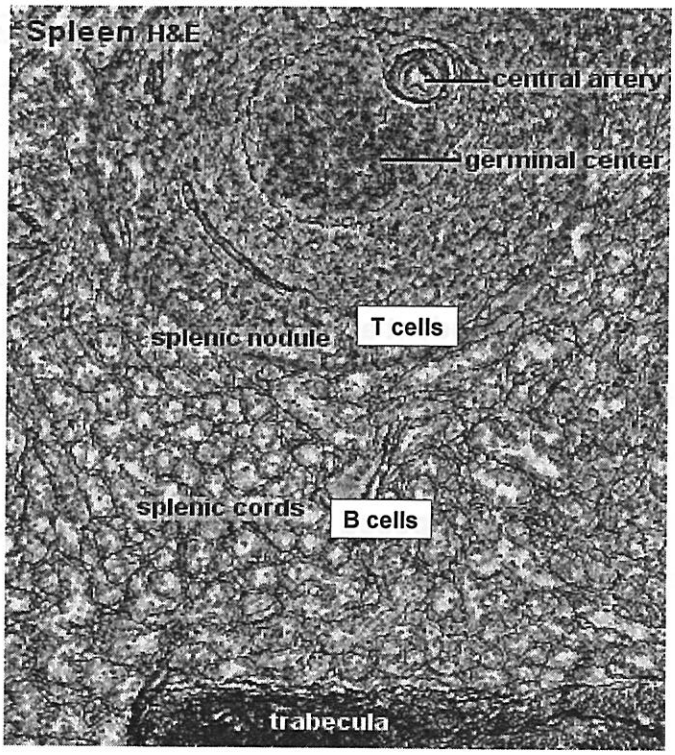
Splenic Nodule in White Pulp



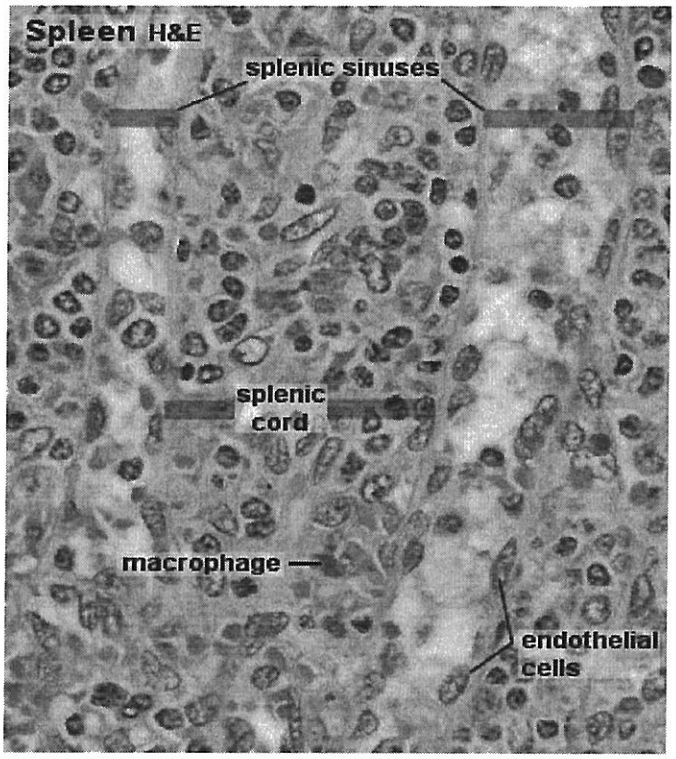
72

- Lymphoid nodules in white pulp may display germinal centers, indicative of antigenic challenge.
- The white pulp is surrounded by a marginal zone that separates the white pulp from the red pulp.
- The marginal zone is composed of plasma cells, T and B lymphocytes, macrophages, and interdigitating dendritic cells (APCs).
- Numerous small vascular channels, marginal sinuses, are present in the marginal zone, especially surrounding lymphoid nodules.

Red Pulp

- The red pulp of the spleen is composed of splenic sinuses and splenic cords (of Billroth).
- The red pulp resembles a sponge, in that the spaces within the sponge represent the sinuses and the sponge material among the spaces denotes the splenic cords.

1. The splenic sinuses
   - are lined with unusual endothelium that cells are fusiform with discontinuous basal lamina and
   - are surrounded by reticular fibers (continuous with those of the splenic cords) that wrap around the sinuses as individual of thin strands of thread.



2. The splenic cords

- **are composed of a loose network of reticular fibers, whose interstices are permeated by extravasated blood.**
- **The reticular fibers are enveloped by stellate reticular cells, which isolate the type III collagen fibers from blood, preventing a platelet reaction to the collagen (coagulation).**
- **Macrophages are particularly numerous in the vicinity of the sinusoids.**

Function of Spleen

- Filters the blood, forms lymphoid cells, eliminates or inactivates blood-borne antigens,
- Destroys aged platelets and erythrocytes, and
- Hemopoiesis.

- As blood enters the marginal sinuses of the marginal zone, it flows past a macrophage-rich zone.
- These cells phagocytose blood-borne antigens, bacteria, and other foreign particulate matter.
- Material that is not eliminated in the marginal zone is cleared in the red pulp at the periphery of the splenic sinuses.

PowerPoint

เรื่อง

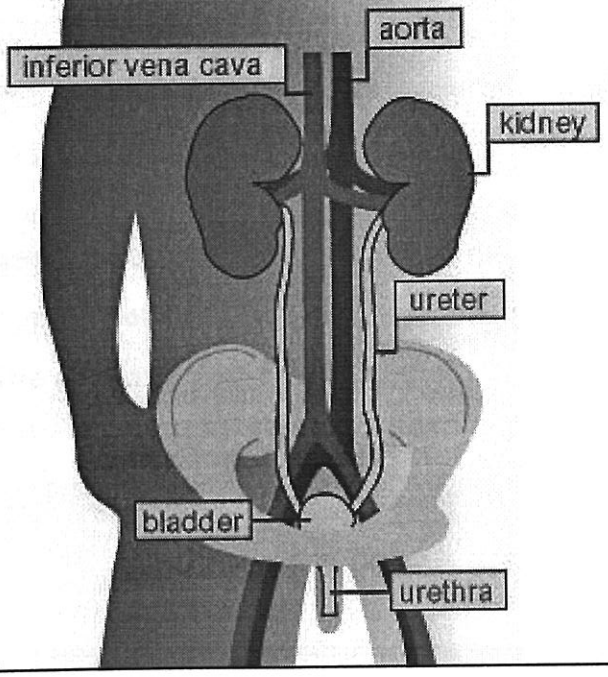
Renal-urinary System

รองศาสตราจารย์ ดร. กรกช อินทราพิเชฐ

Renal / Urinary System

The urinary system removes toxic by-products of metabolism from the bloodstream and removes urine from the body.

1



2

Urinary System

- Paired kidneys & ureters and unpaired bladder & urethra
- The Urinary System maintains homeostasis
  - Regulation of levels of ions such as sodium, potassium, chloride, and calcium
  - Regulation of the water content of the blood
  - Maintaining proper pH of the blood
- The system helps to maintain homeostasis by the complex processes that involves filtration, active absorption, passive absorption, and secretion.

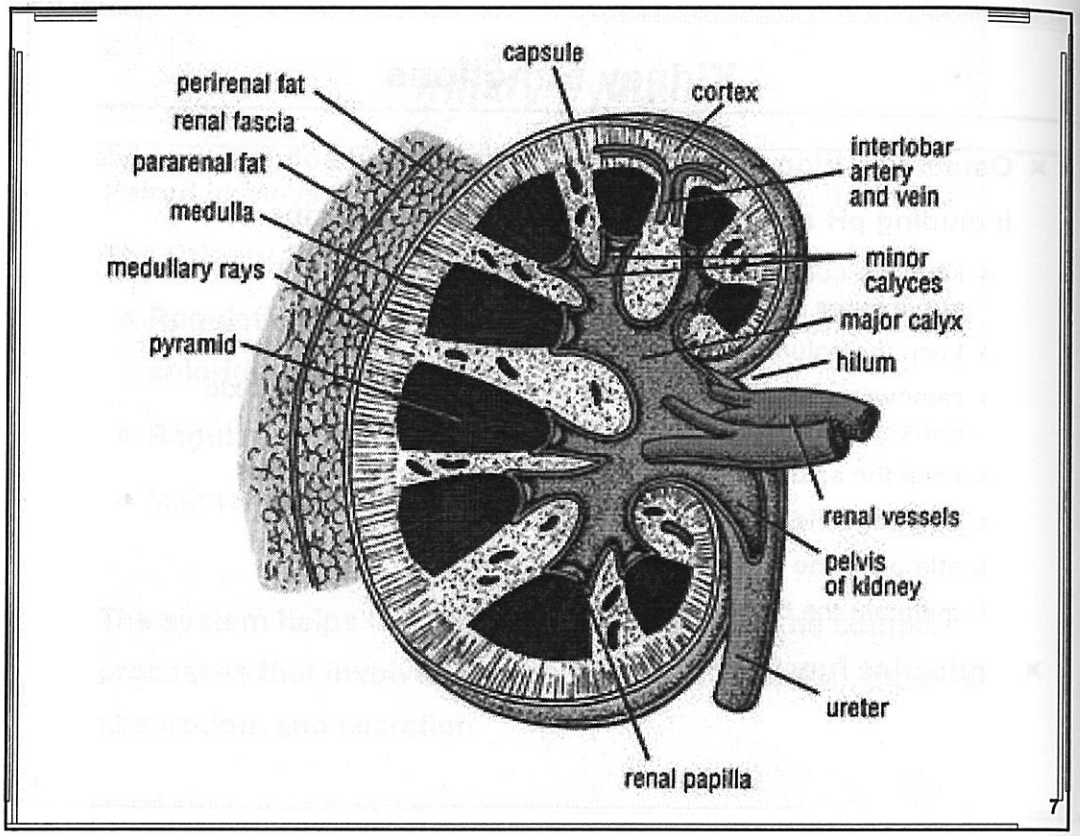
Kidneys

Kidney Functions

- Osmoregulation – regulates body's water and solute (electrolyte) including pH and produces ultrafiltrate called urine
  - keep the concentrations of various ions and other important substances constant
  - keep the volume of water in body constant
  - remove wastes from the body (urea, ammonia, drugs, toxic substances)
  - keep the acid/base concentration of blood constant (pH)
  - help regulate the blood pressure
  - stimulate the making of red blood cells
  - maintain the body's calcium levels
- Endocrine function

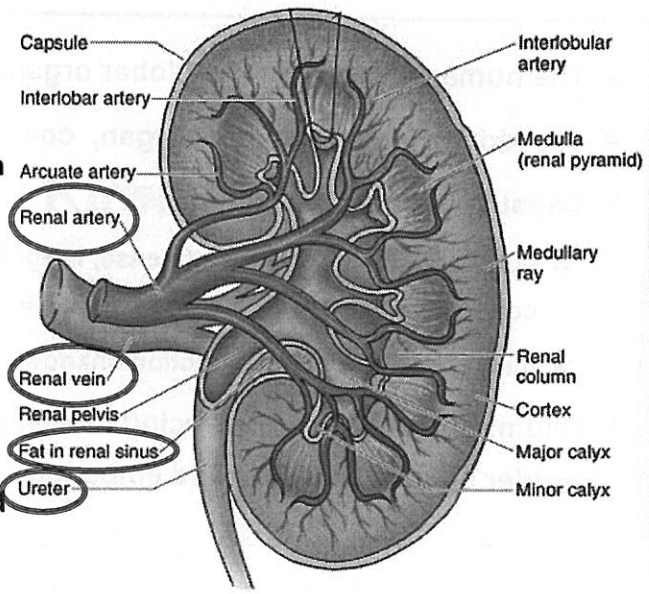
Kidney Structure

- The human kidney is a multilobar organ.
- The kidney is bean-shaped organ, covered with capsule.
- Capsule is bi-laminar (humans)
  - outer: consisting mainly of dense, irregular collagenous connective tissue with occasional elastic fibers and
  - inner: myofibroblasts; function unknown
- Hilum: The concave area facing medially on the convex border situated laterally and embedded in perirenal fat.



7

- **Hilum is the area where;**
  - **Branches of the renal artery and vein, lymph vessels, and ureter enter the kidney.**
  - **A fat-filled extension of the hilum deeper into the kidney is called the renal sinus.**
- **The ureter is expanded forming the renal pelvis.**



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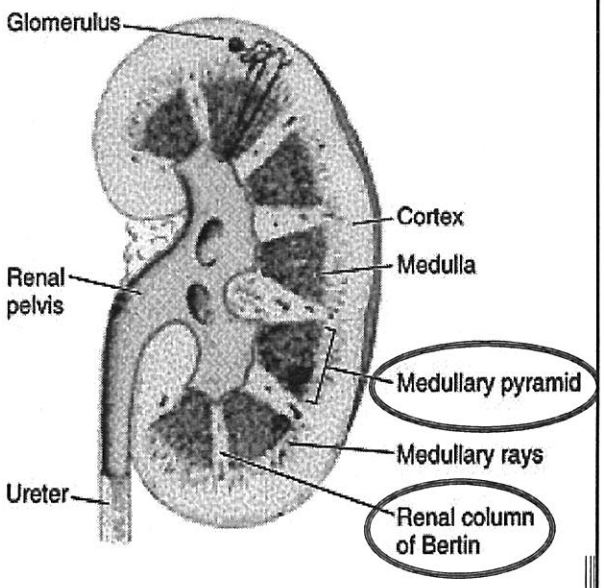
Kidney Structure (cont.)

- The parenchyma of the kidney can be divided into 2 regions
- Cortex – outer region, dark brown & granular in apperaance
- Medulla – inner region, contains 10 to 18 pyramidal structures, the renal pyramids / medullary pyramids, between pyramids is the cortical columns of Bertin.



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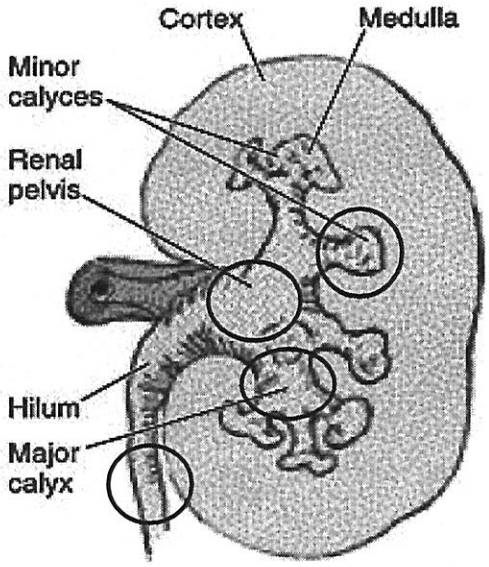
Kidney Structure (cont.)

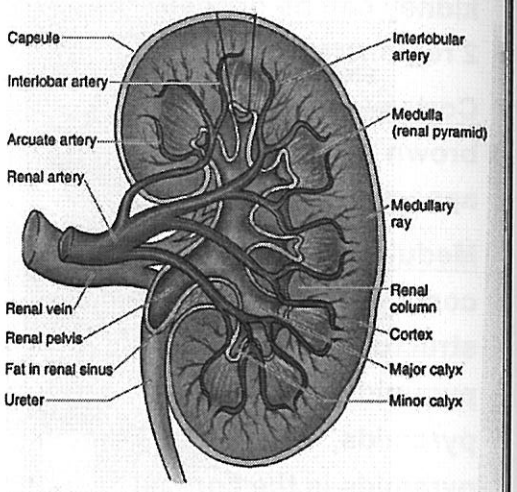
- The apex is surrounded by a cup-like minor calyx, which, joining 2-3 neighboring minor calyces, forms a major calyx.
- The three or four major calyces are larger subdivisions that empty into the renal pelvis, the expanded continuation of the proximal portion of the ureter.



10

Renal Cortex

- The portion of the cortex overlying the base of each pyramid is known as a cortical arch.
- Macroscopically, the cortex has three types of substances
  1. renal corpuscles,
     the red, dot-like granules,
  2. cortical labyrinth,
     the convoluted tubules;
  3. medullary rays, longitudinal striations, which continues to renal pyramids.

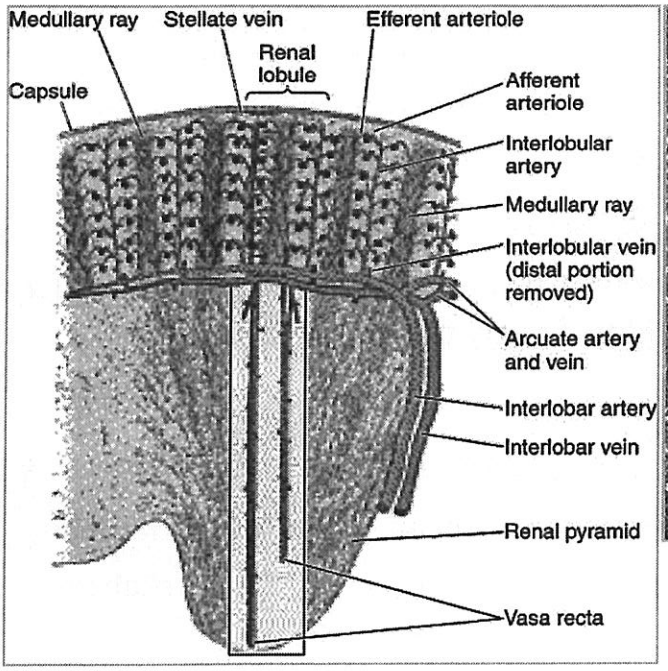


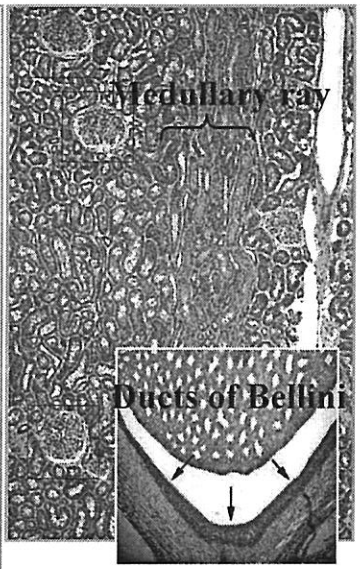
11

Renal Medulla

- The inner region with 10-18 conical structures / renal pyramids.
- A renal pyramid, with its associated cortical arch and cortical columns, represents a lobe of the kidney.
- Each medullary ray with part of the cortical labyrinth surrounding it is considered a kidney lobule, which continues into the medulla as a cone-shaped structure.
- The apex of pyramid is perforated by 20 or so openings of the ducts of Bellini; this sieve-like region is known as the area cribrosa.

12

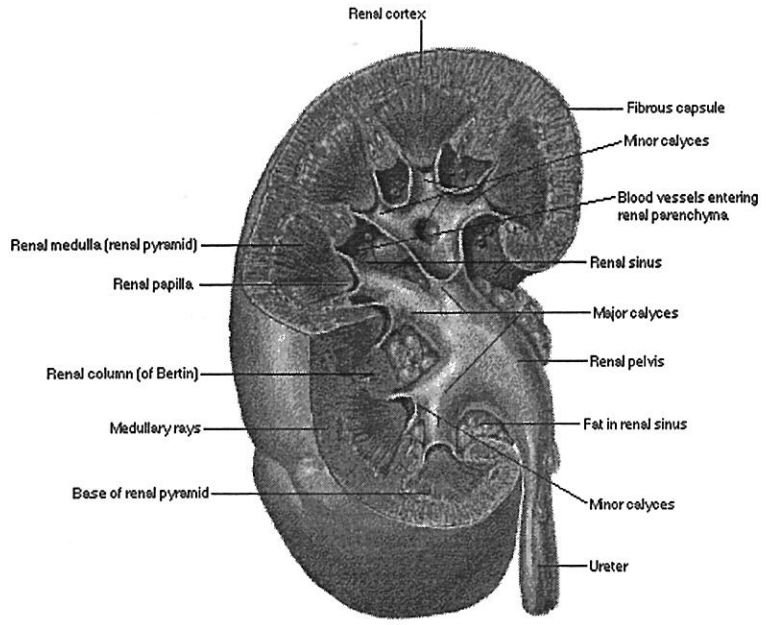




Area Cribrosa

13

Right Kidney Sectioned in Several Planes



14

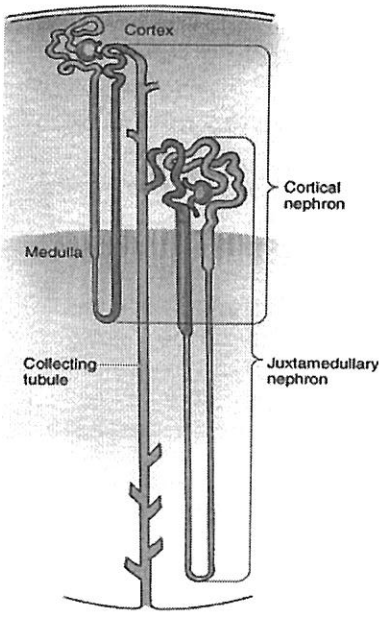
Uriniferous Tubules

The functional unit of the kidney

15

Uriniferous Tubules

- The uriniferous tubule, the functional unit of the kidney, forming urine, is composed of a
  - 1. Nephron and
  - 2. Collecting tubule
- Each kidney contains of 1-4 million nephrons.



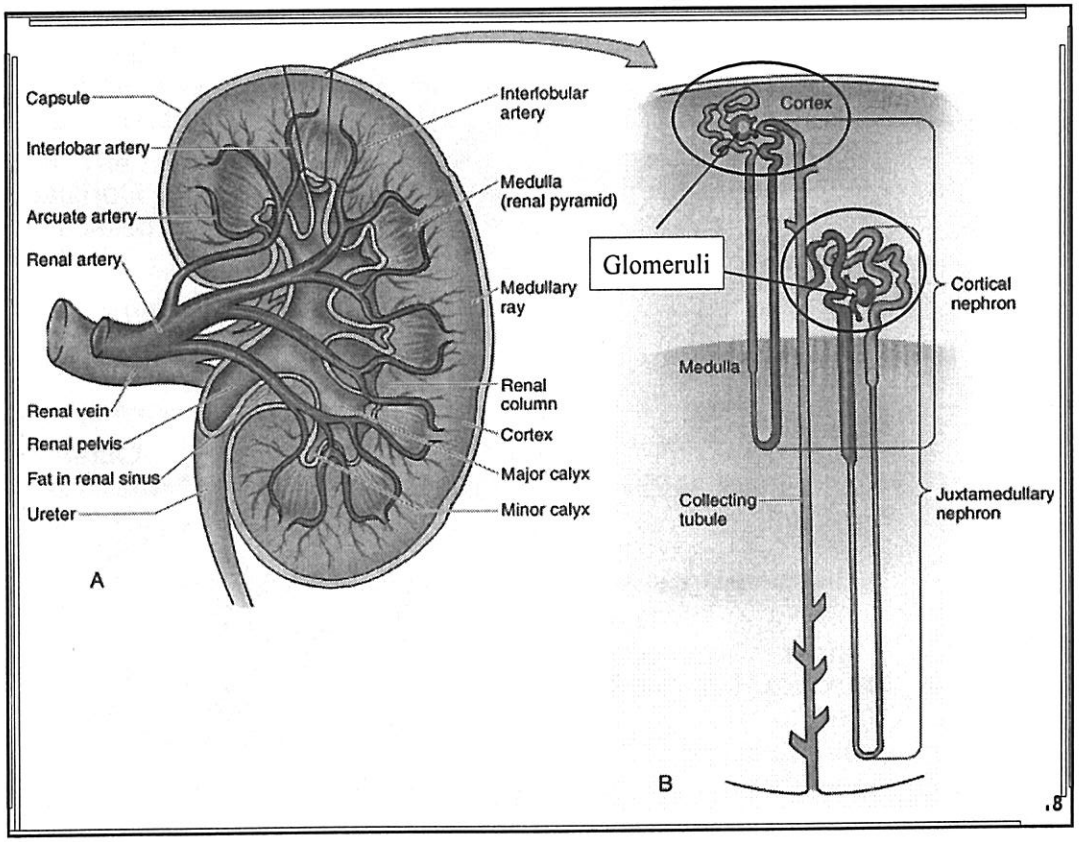
16

Nephrons

- In the human kidney, there are 2 types of nephrons, depending on the location of their renal corpuscles and the length of their Henle's loop.

1. Cortical nephrons, shorter, subdivided into two groups, superficial and midcortical nephrons, neither of which extend deep into the medulla,
2. Juxtamedullary nephrons, longer, renal corpuscle is located in the cortex and whose tubular parts extend deep into the medulla.

17



18

Nephrons (cont.)

- Each nephron consists of
  1. renal corpuscle;
  2. proximal tubule;
  3. thin & thick limbs of Henle's loop;
  4. distal tubule;
  [5. collecting tubules & ducts.]
- The entire uriniferous tubule is epithelial in nature and is separated from the connective tissue stroma by an intervening basal lamina.

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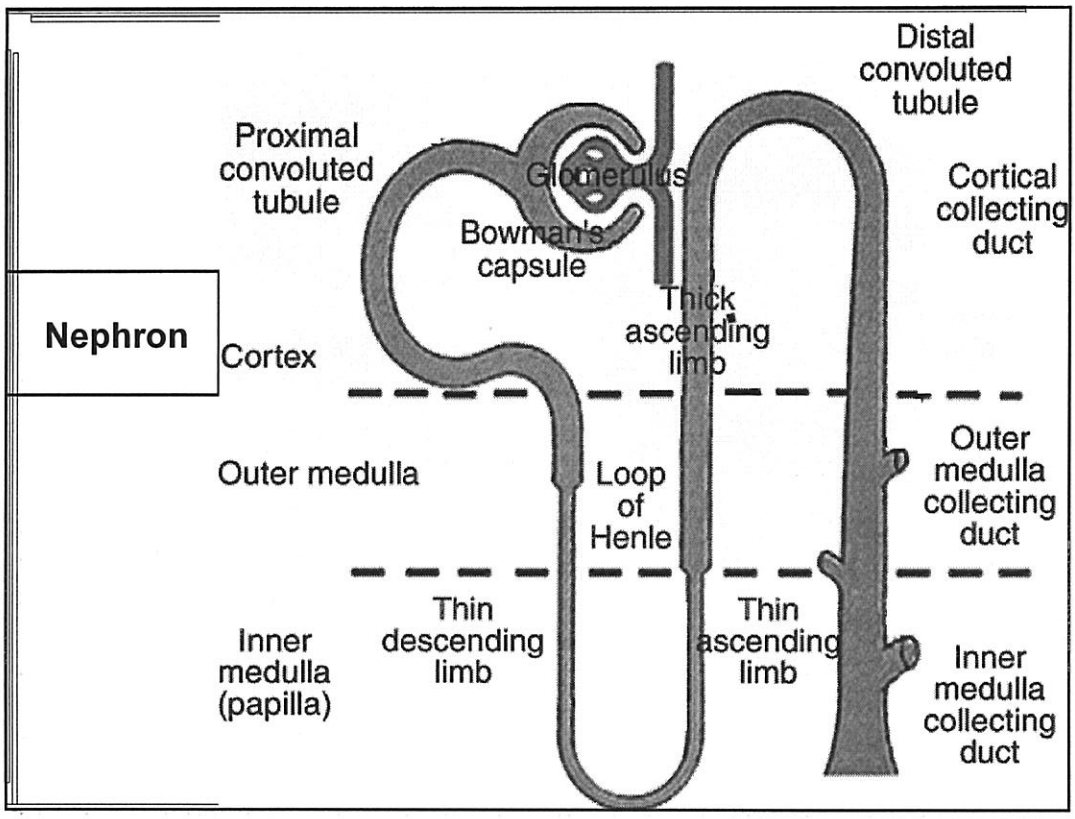
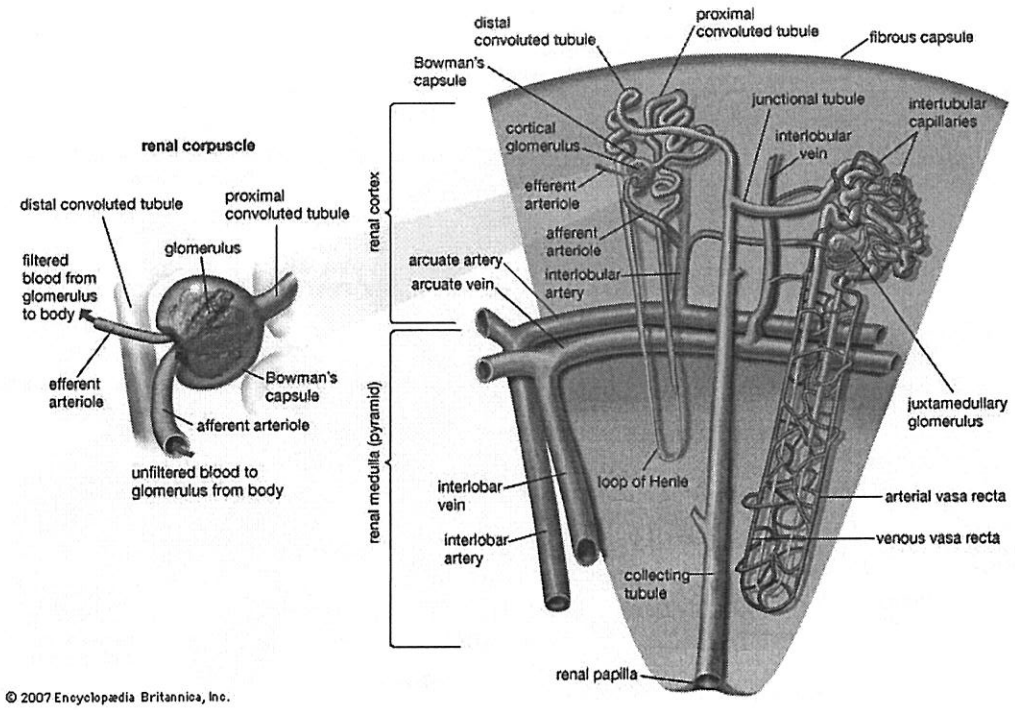




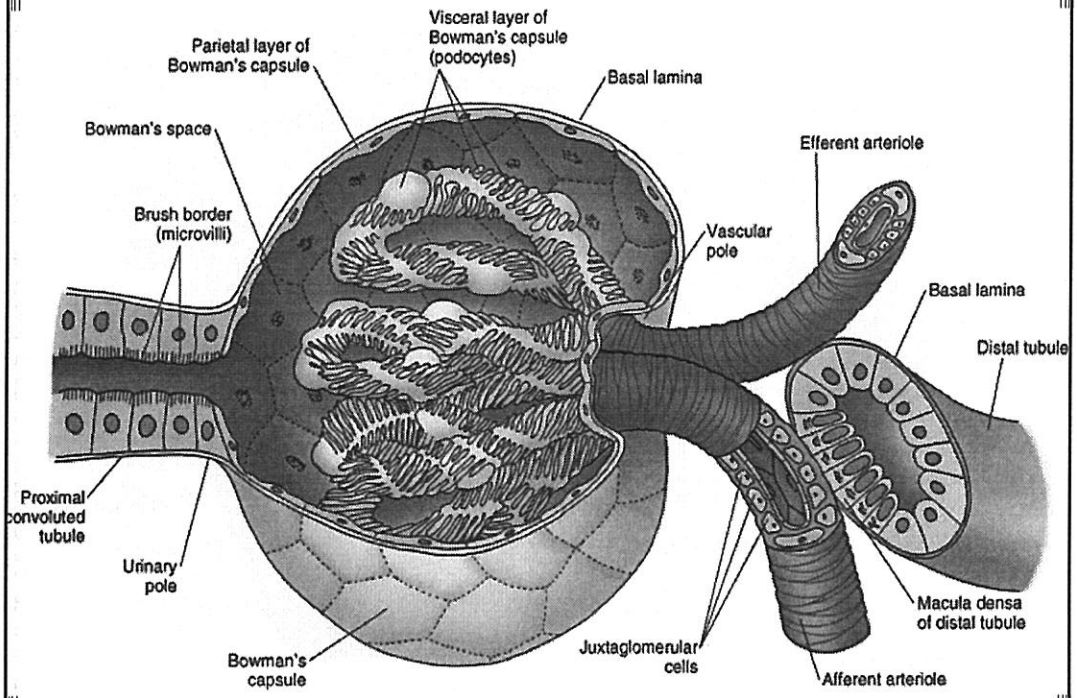
21

1. Renal Corpuscle

- The renal corpuscle is composed of;
  - 1.1 Glomerulus, a tuft of capillaries
  - 1.2 Bowman's capsule with 2 layers separated by Bowman's space (urinary space).
- The renal corpuscle, an oval to round structure about 200 to 250 µm in diameter.
- Bowman's capsule is the pouch-like, proximal end of the nephron composed of two layers:
  - 1.2.1 Visceral layer (inner layer) of large & highly modified epithelial cells called podocytes.
  - 1.2.2 Parietal layer (outer wall) is surrounded by simple squamous epithelium, lining the capsule.

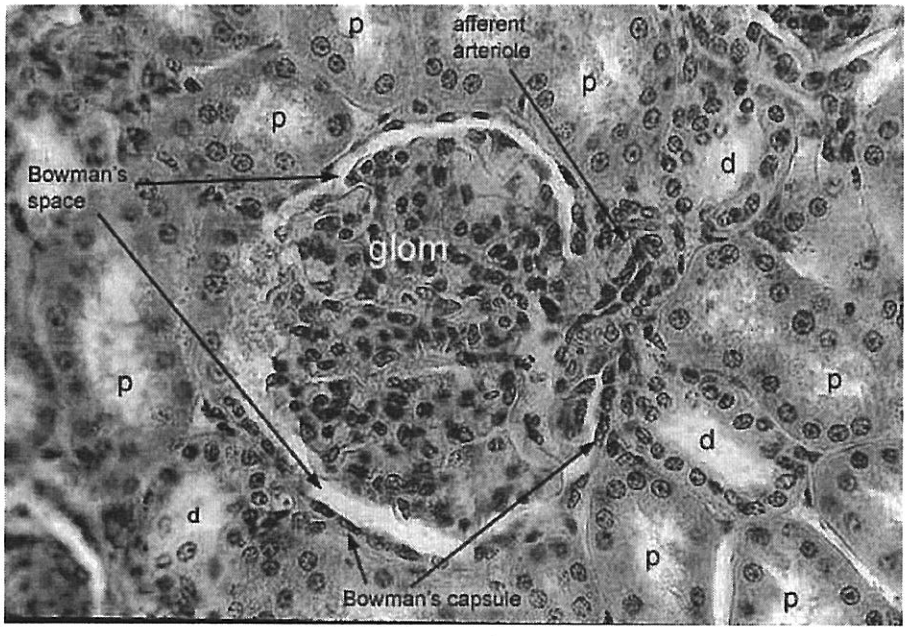
22

Renal Corpuscle



23

Renal Corpuscle



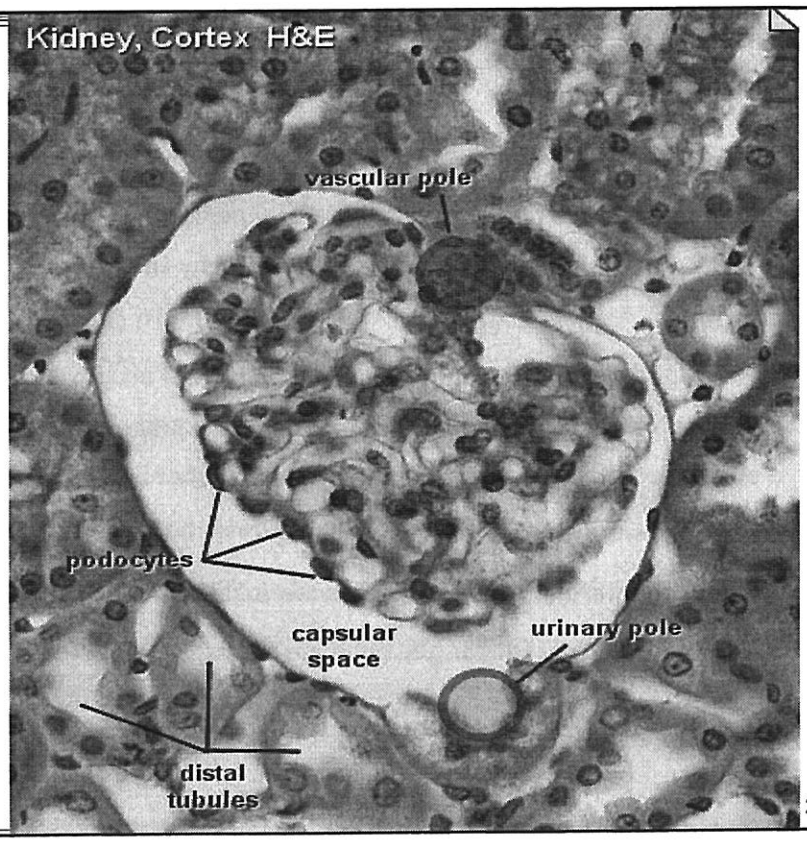
24

Renal Corpuscle (cont.)

- The vessels supplying and draining the glomerulus enter and exit Bowman's capsule is known as the vascular pole,
- The region of continuation between the renal corpuscle and the proximal tubule, drains Bowman's space, is called the urinary pole.
- Blood supply to glomerulus by afferent glomerular arteriole and drained by the efferent glomerular arteriole; thus the glomerulus is a completely arterial capillary bed.

25

Renal Corpuscle



26

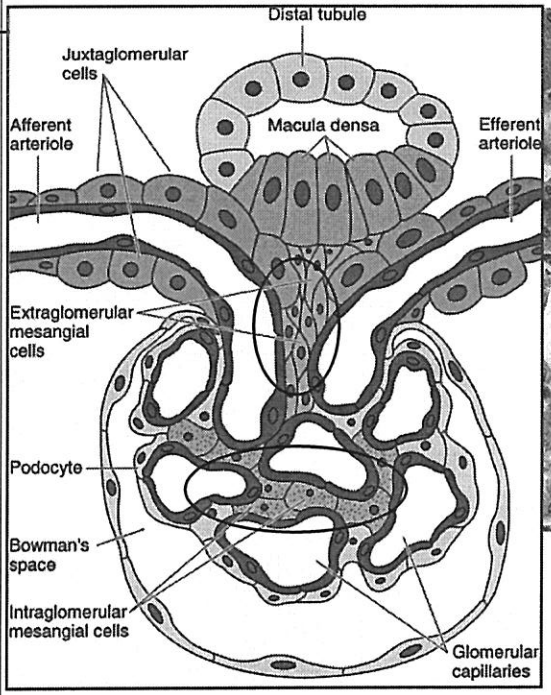
Renal Corpuscle (cont.)

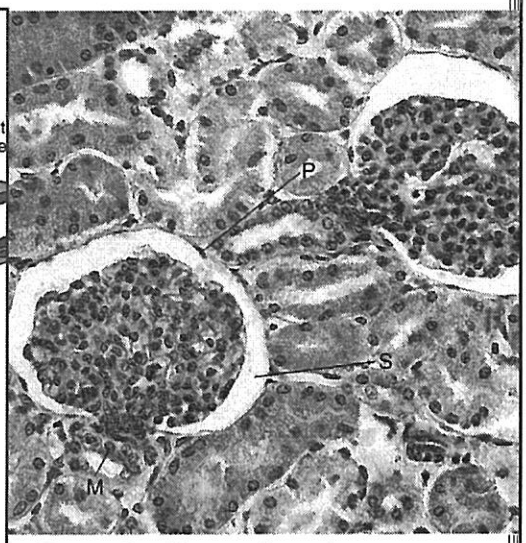
- The efferent glomerular arteriole presents greater resistance to blood flow, resulting in higher capillary pressures in the glomerulus than in other capillary beds.
- Filtrate leaking out of the glomerulus enters Bowman's space through a complex filtration barrier
- Filtration barrier is composed of
  - 1. the endothelial wall of the capillary,
  - 2. the basement membrane / basal lamina of endothelial cell & of podocyte, and
  - 3. the visceral layer of Bowman's capsule (pedicel of podocyte).

Glomerulus

- The glomerulus is composed of tufts of fenestrated capillaries supplied by the afferent glomerular arteriole and drained by the efferent glomerular arteriole.
- The connective tissue component of the afferent arteriole does not enter Bowman's capsule, and the normal connective tissue cells are replaced by a specialized CT cell type known as mesangial cells.
- There are two groups of mesangial cells:
  - extraglomerular mesangial cells are located at the vascular pole,
  - intraglomerular mesangial cells are situated within the renal corpuscle, probably phagocytic and function in resorption of the basal lamina.

Glomerulus





P = parietal layer ; S = urinary space ;

M = macula densa

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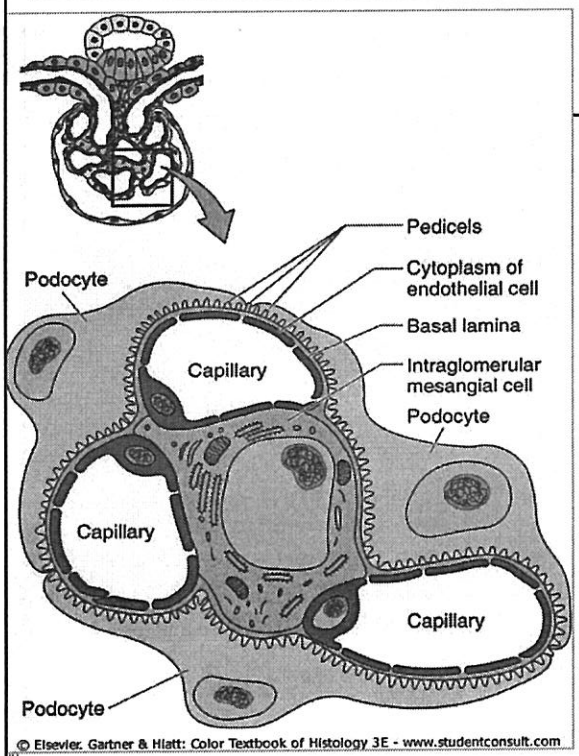
Glomerulus (cont.)

- **Mesangial cells may also be contractile because they have receptors for vasoconstrictors such as angiotensin II and thus reduce blood flow through the glomerulus.**
- **Mesangial cells, along with podocytes and the glomerular basement membrane, provide physical support to the capillaries of the glomerulus.**
- **Capillary of the glomerulus: fenestrated capillaries. whose endothelial cells are highly thin, except for the region containing the nucleus; their fenestrae are usually not covered by a diaphragm.**
- **The fenestrae are large, ranging between 70 and 90 nm in diameter; hence, these capillaries act as a barrier only to formed elements of the blood and to macromolecules whose effective diameter exceeds the size of the fenestrae.**

30



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Renal Filter Membrane

- Renal Filter Membrane is formed by
    1. Endothelial cells of Capillary
    2. Podocytes

Renal Filter Membrane =

1. Glomerular Basement Membrane
2. Basement Membrane of Visceral layer of Bowman's capsule

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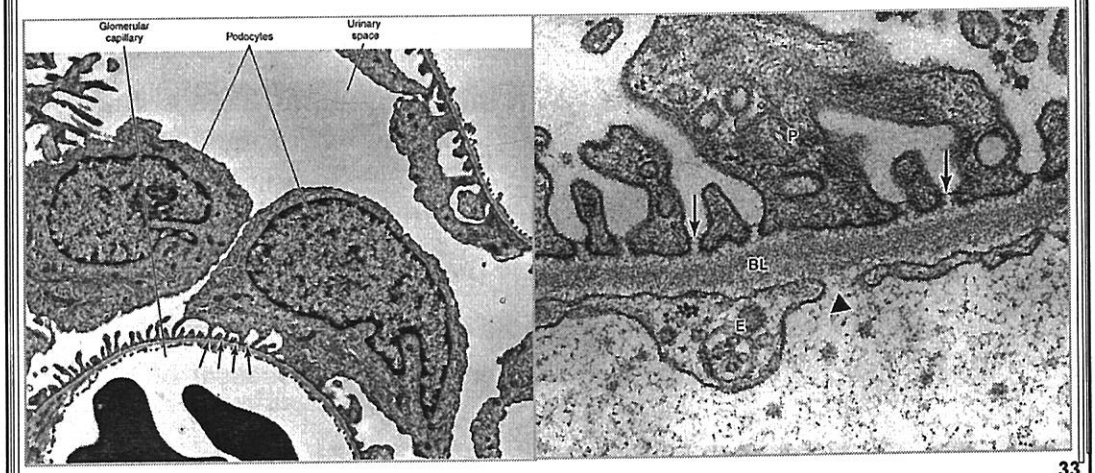
Glomerular Basement Membrane

- Glomerular basement membrane (~300 nm thick), is derived from the fusion of capillary- and podocyte-produced lamina
- This membrane is the filtration barrier that separates the urine space and the blood in the capillary.



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Glomerular Basement Membrane (cont.)

- The basement membrane consisting of three layers;
  1. Lamina densa, middle dense layer, is about 100 nm in thickness, consists of collagen type IV with negatively charged proteoglycan heparan sulfate.
     - Laminae rarae, less electron-dense layers, contain laminin and fibronectin for attachment of pedicels & endothelial cells, and polyanionic proteoglycans perlacan and heparan sulfate
  2. lamina rara interna, between the endothelial cells of the capillary and the lamina densa,
  3. lamina rara externa, between the lamina densa and the visceral layer of Bowman's capsule (Podocytes).

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Glomerular Basement Membrane (cont.)

- The visceral layer of Bowman's capsule of podocytes, modified epithelial cells.
- Podocytes have numerous long, tentacle-like cytoplasmic extensions, primary (major) processes, that follow but usually do not come in close contact with the longitudinal axes of the glomerular capillaries
- Each primary process bears many secondary processes, known as pedicels, arranged in an orderly fashion.
- Pedicels completely envelop most of the glomerular capillaries by interdigitating with pedicels from neighboring major processes of different podocytes.

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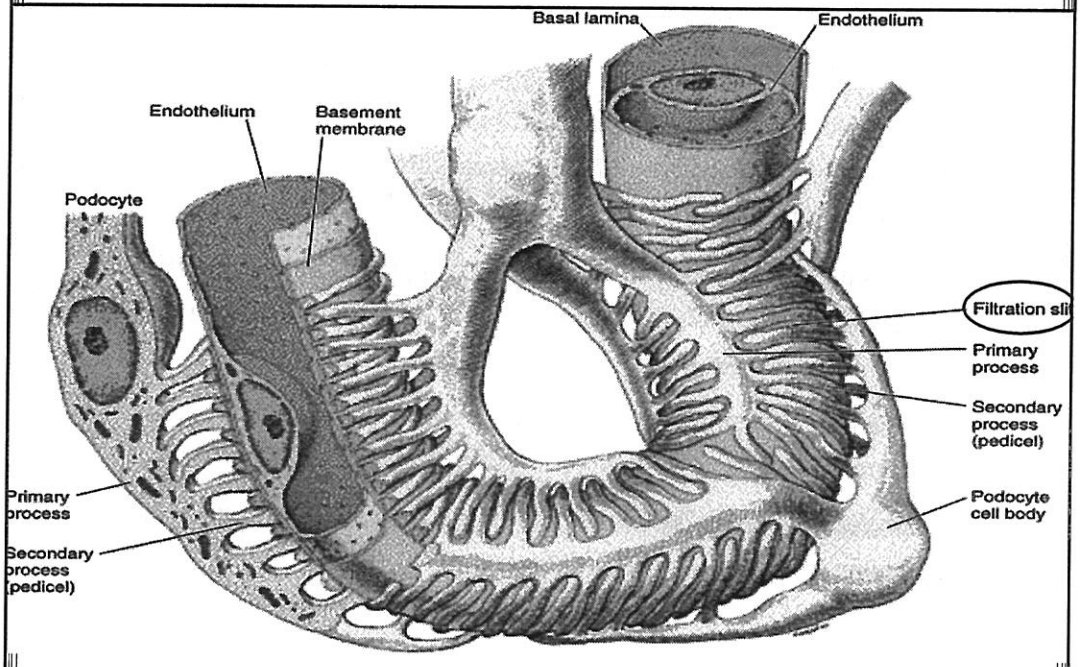
Glomerular Basement Membrane (cont.)



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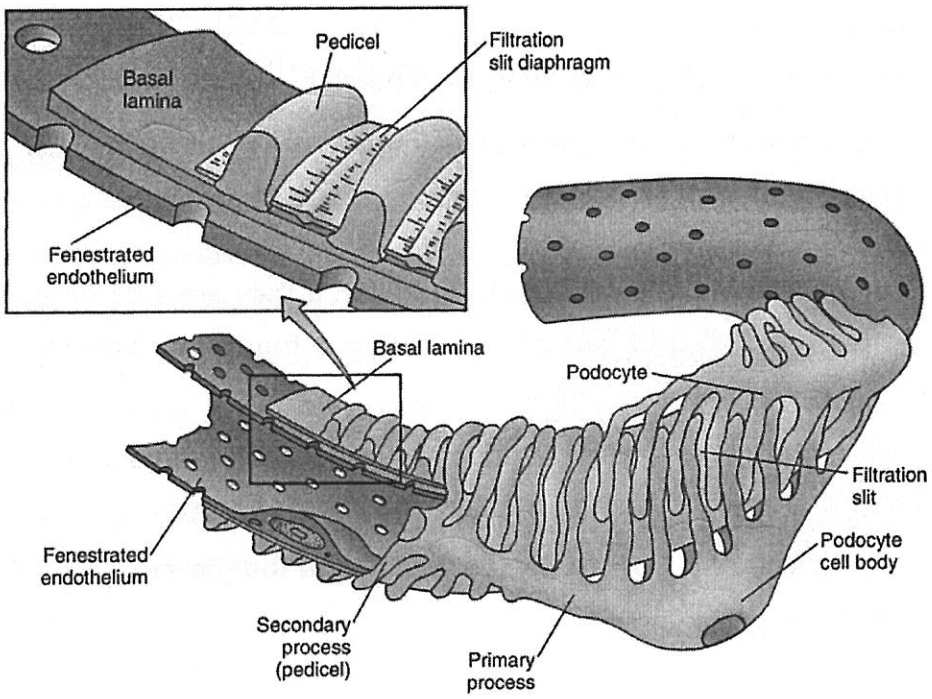
Glomerular Basement Membrane (cont.)

- Pedicels have a well-developed glycocalyx.
- Pedicels rest on the lamina rara externa of the basal lamina.
- Interdigitation of pedicel occurs in such a fashion that narrow clefts, 20 to 40 nm in width, known as filtration slits, remain between adjacent pedicels.
- Filtration slits are not completely open; instead, they are covered by a thin slit diaphragm and has a central bar on either side of which are rows of pores 14 nm^2 in area
- The slit diaphragm extends between neighboring pedicels and acts as a part of the filtration barrier.

Filtration barrier in the Visceral layer of Bowman's capsule



Blood Filtration

- Fluid leaving the glomerular capillaries through the fenestrae is filtered by the basal lamina.
- Lamina densa is the meshwork of type IV collagen and lamina in a matrix containing negatively charged proteoglycan heparan sulfate that restricts the passage of cationic molecules and traps proteins with molecular mass greater albumin (> 69,000Da).
- Fluid, which contains small molecules, ions, and macromolecules, penetrates the lamina densa and must pass through the pores in the slit diaphragm of the filtration slits.

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Blood Filtration (cont.)

- The lamina densa acts as a physical barrier.
- The laminae rarae with polyanions impede the passage of negatively charged molecules, acts as charge barrier.
- If the macromolecules are uncharged and if they are 1.8 nm or less in diameter, they can pass without any hindrance through the slit diaphragm.
- If the uncharged macromolecules are greater than 4 nm in diameter they cannot pass through the slit diaphragm.
- The fluid entering Bowman's space is called the glomerular ultrafiltrate.

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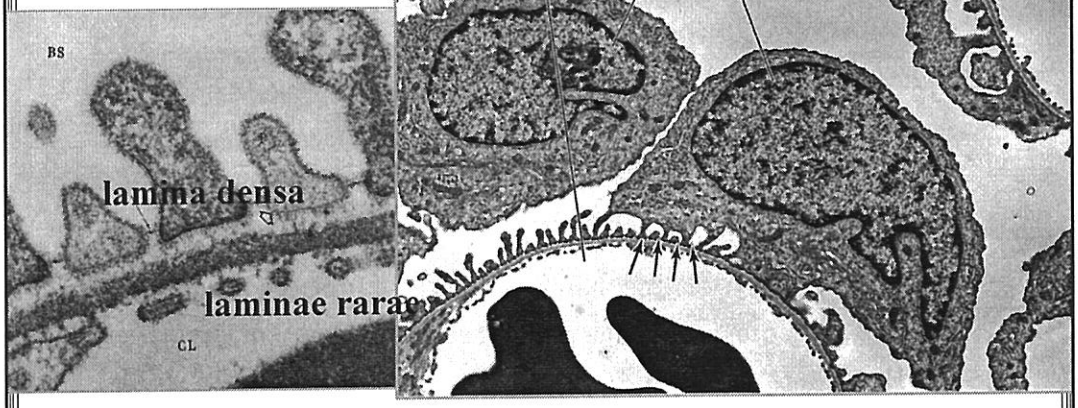
Blood Filtration (cont.)

- Filtration barrier
  - Physical barrier
  - Charge barrier



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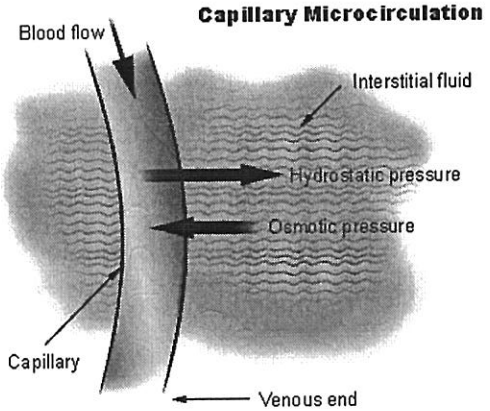
- Osmosis: Solvent passes through membrane
- Dialysis: Solute passes through membrane
- Osmotic pressure: This term refers to the physical pressure that exists between two aqueous solutions with different concentrations of a particular solute which are separated by a membrane that allows water to pass freely through it but not what is in solution.
- Hydrostatic pressure: The physical force that ultimately results in a net pushing out of fluid (filtration) from the capillary to the interstitial space.
- Oncotic pressure applied by the plasma proteins induced osmotic pressure



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Blood Filtration (cont.)

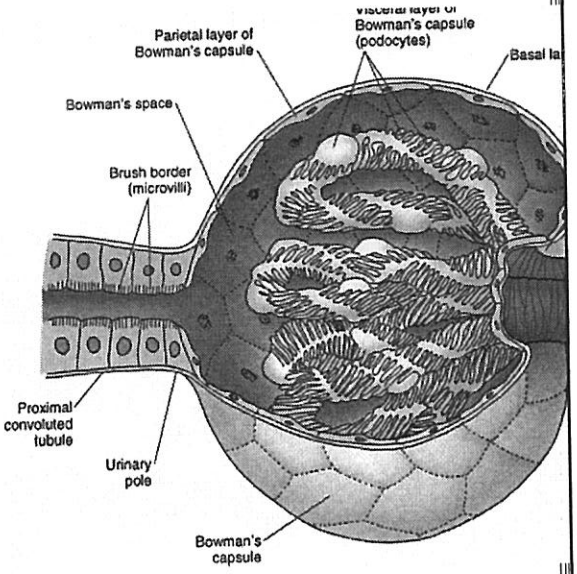
- Hydrostatic pressure in the arterial capillaries is about 45 mmHg which is higher in the other capillaries.
- The glomerular filtrate is formed in response to the hydrostatic pressure of blood, which opposed to
  - (1) the osmotic (oncotic) pressure of the plasma colloids (200 mm Hg), and
  - (2) the hydrostatic pressure of the fluids in Bowman's capsule (10 mm Hg).
- The net filtration pressure at the afferent end of glomerular capillaries is 15 mm Hg.

Blood Filtration (cont.)

- The glomerulus filtrate has a chemical composition similar to that of blood plasma but contains almost no protein, because macromolecules do not readily cross the glomerular filter.
- The large protein molecules that succees in crossing the glomerular filter have a molecular mass of about 70 kDa, and small amounts of plasma albumin appear in the filtrate.
- The basal lamina traps larger macromolecules, it would become clogged were it not continuously phagocytosed by intraglomerular mesangial cells and refilled by both the visceral layer of Bowman's capsule (podocytes) and glomerular endothelial cells.

2. Proximal tubule

- Bowman's space drains into the proximal tubule at the urinary pole.
- The simple squamous epithelium of the parietal layer of Bowman's capsule joins the simple cuboidal epithelium of the proximal tubule
- The proximal tubule, constituting much of the renal cortex.



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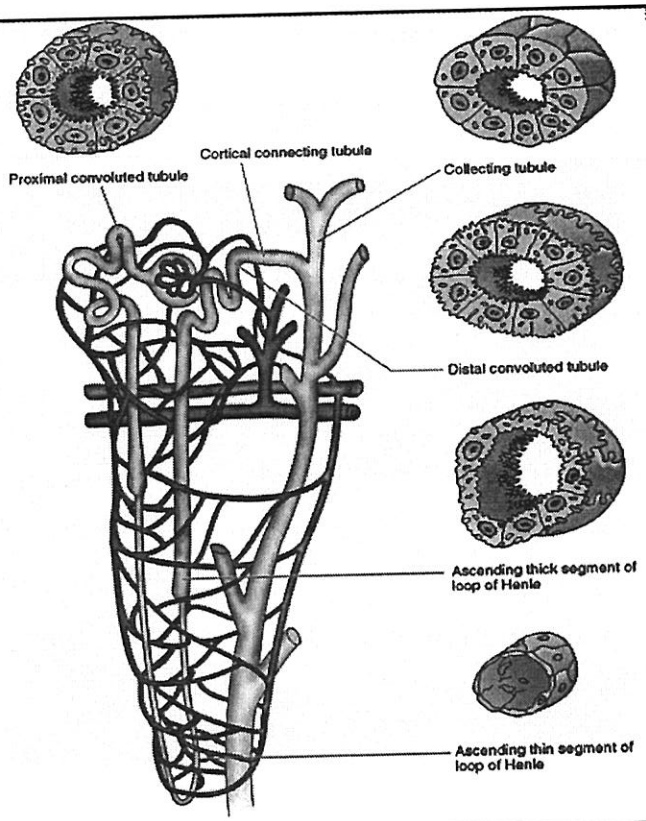
Renal Tubules



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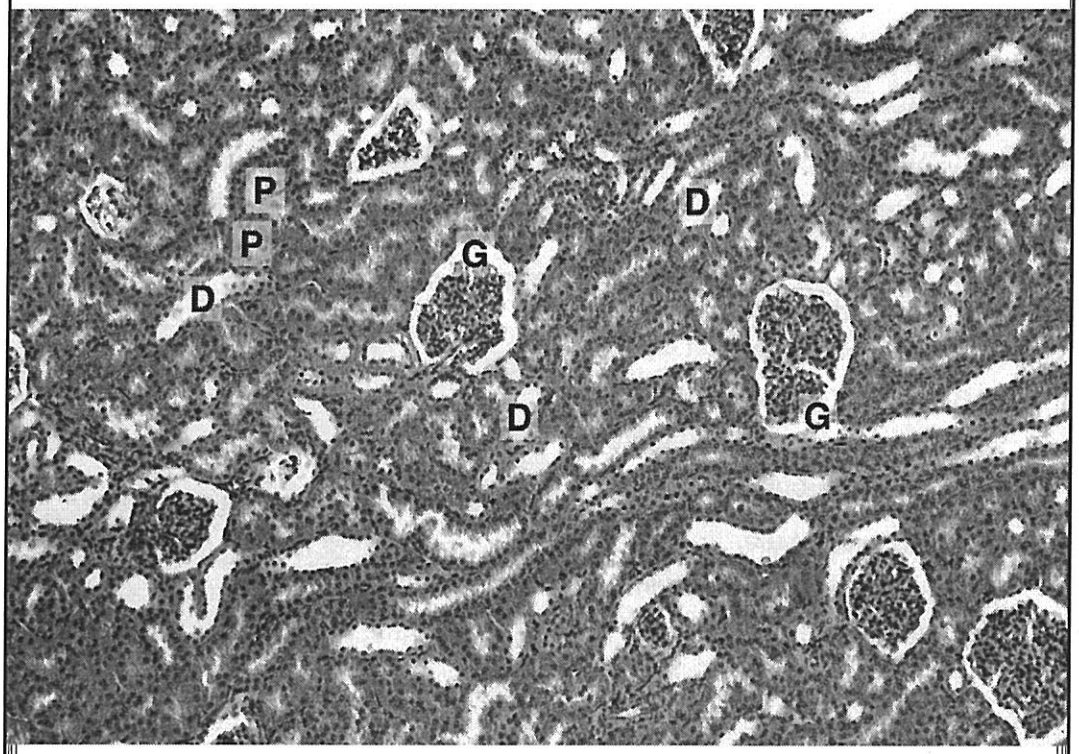

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Proximal tubule (cont.)

- Proximal tubule consists of a highly tortuous region, is approximately 60 μm in diameter and about 14 mm long.

1. Pars convoluta (proximal convoluted tubule), located near renal corpuscles, and a straighter portion,
2. Pars recta (descending thick limb of Henle's loop), which descends in medullary rays within the cortex and then in the medulla to become continuous with the loop of Henle at the junction of the outer and inner stripes.

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Proximal tubule (cont.)

- The convoluted portion is composed of a simple cuboidal epithelium with brush border and an intricate system of intercalation.
- The height of the cells varies with their functional state from a low cuboidal to an almost high cuboidal epithelium.
- This system is more extensive during active diuresis, suggesting that it functions in resorption of proteins during tubular clearing of the glomerular ultrafiltrate.

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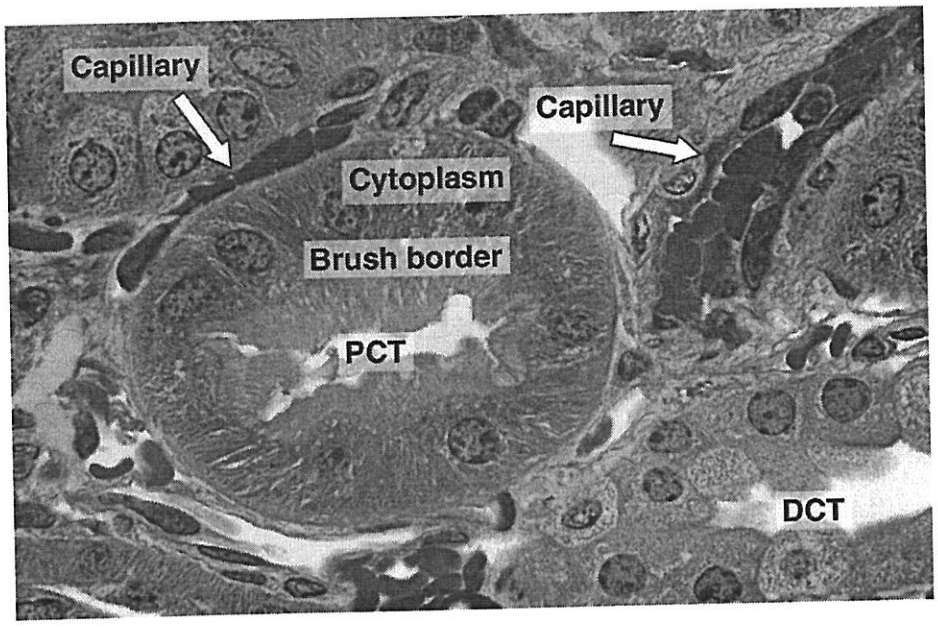
Proximal tubule



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Selective Reabsorption of Glomerular Ultrafiltrate at Proximal Tubule

- About 67% to 80% of Na^+, Cl^-, and H_2O is resorbed by cells of the proximal tubule.
  - Reabsorption of Na^+ is actively pumped out of the cell at the basolateral cell membranes by Na^+, K^+-ATPase.
  - Reabsorption of Cl^- to maintain electrical neutrality.
  - Reabsorption of H_2O to maintain osmotic equilibrium.
- The water passes through aquaporin-1 channels located in the basolateral cell membrane.
- All of the glucose, amino acids, and protein in the glomerular ultrafiltrate are resorbed by endocytosis.
- The proximal tubule also eliminates the organic solutes, drugs, and toxins that must be rapidly excreted from the body.

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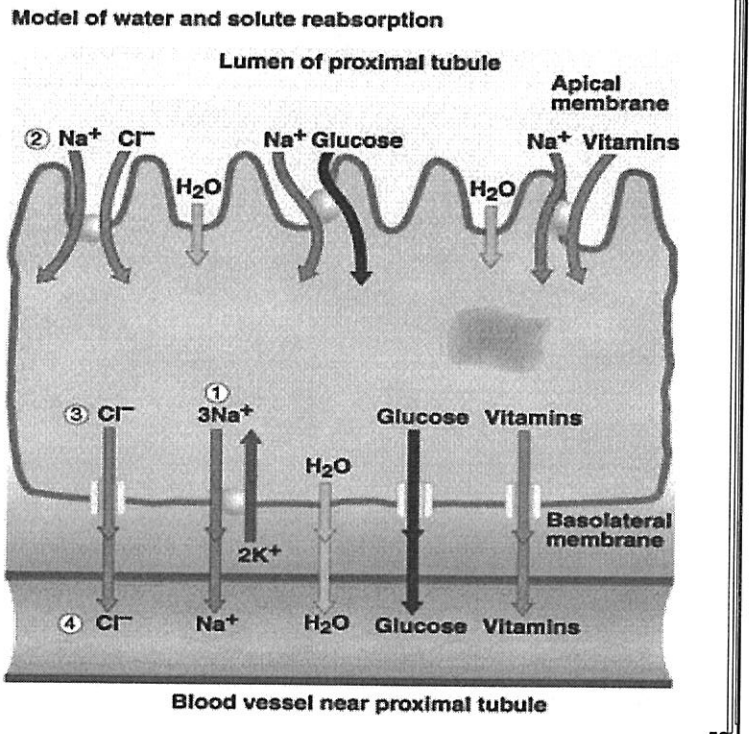
Reabsorption Function of Proximal Tubule



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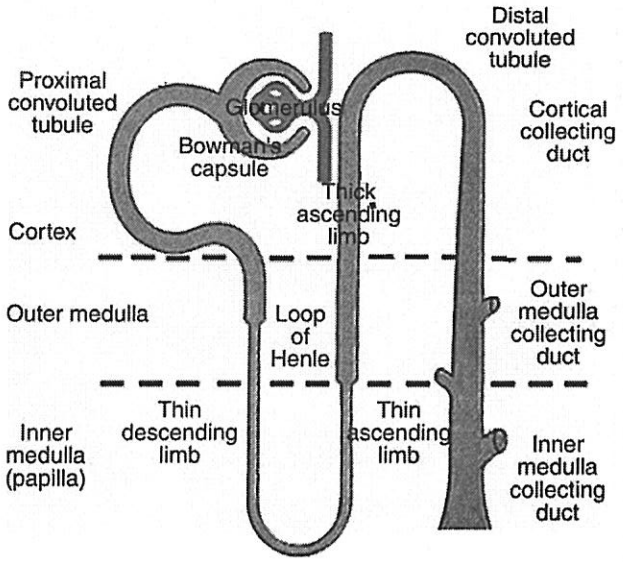
3. Henle's Loop

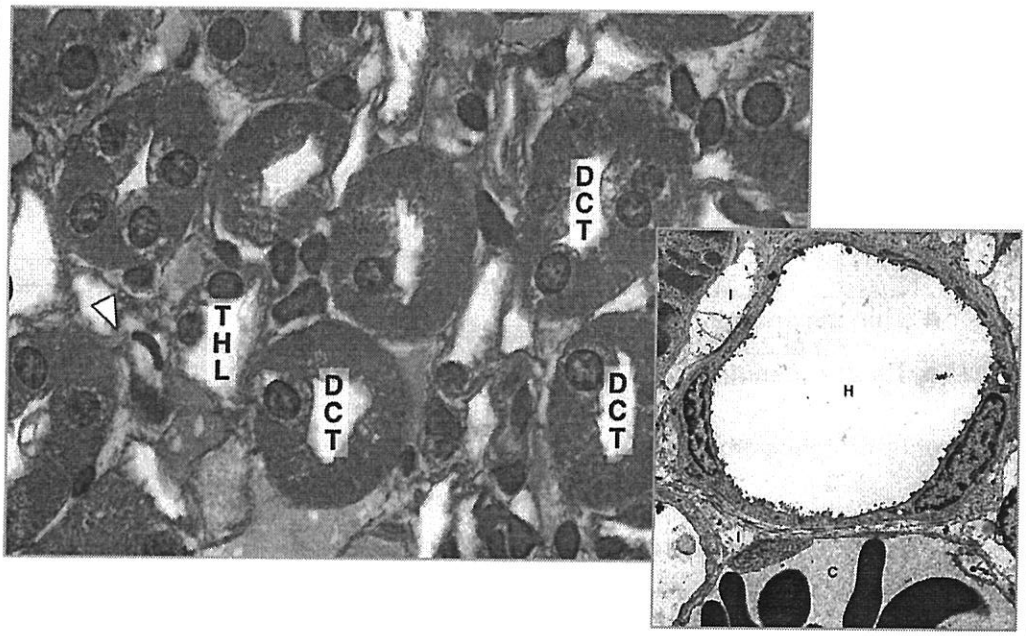
- U-shaped structure, consisting of
  - Thick descending limb
  - Thin descending limb
  - Thin ascending limb
  - Thick ascending limb



Henle's loop (cont.)

- Thick tubule is about 60 μm, is composed of cuboidal epithelial cells
- Thin tubule, about 15 to 20 μm, is composed of squamous epithelial cells with an average height of 1.5 to 2 μm.
- Cortical nephrons, the thin segment is only 1 to 2 mm long or may be completely absent.
- Juxtamedullary nephrons have much longer thin segments, 9 to 10 mm in length, and they form a hairpin-like loop that extends deep into the medulla as far down as the renal papilla.
- Henel's loop is involved in water retention of body; capable of producing hypertonic urine and maintaining body water.

Henle's loop



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Henle's loop (cont.)

- HL creates a gradient of hypertonicity in the medullary interstitium that influences the concentration of urine as it flows through the collecting ducts.
- Thin descending limb is freely permeable to water due to the presence of numerous aquaporin-1 water channels.
- Thin ascending limb is impermeable / moderately permeable to water.
- Thick ascending limb active transports Na^+ & Cl^-, creates gradient of hypertonicity on medullary interstitium.

  It is reasonably permeable to urea, sodium, chloride, and other ions.

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4. Distal Tubule

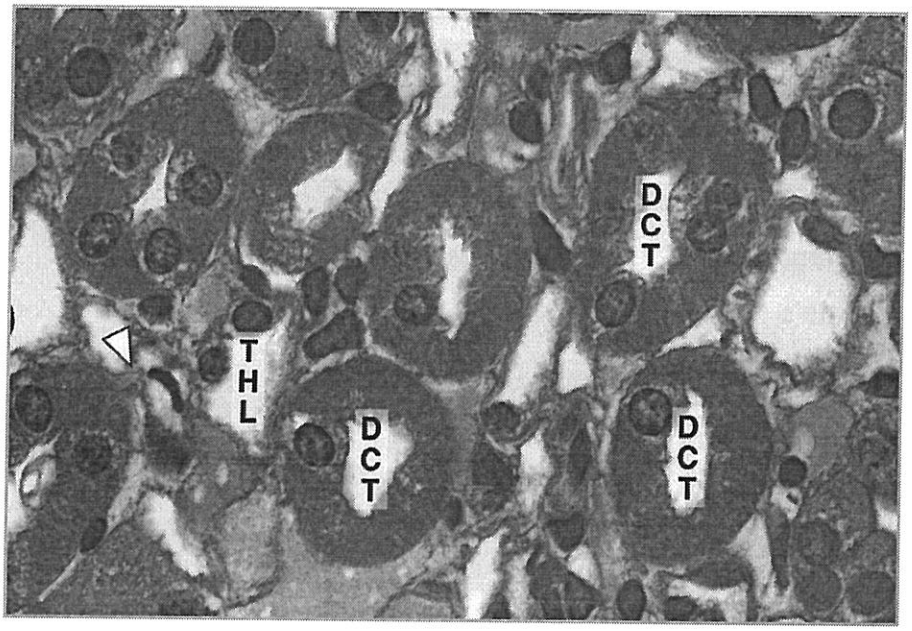
- The distal tubule is subdivided into

1. Pars recta, which is the continuation of the ascending thin limb of Henle's loop, is also known as the ascending thick limb of Henle's loop, and
2. Pars convoluta (distal convoluted tubule). Interposed between the ascending thick limb and the distal convoluted tubule is a modified region of the distal tubule called the macula densa.

Pars recta / Ascending thick limb of Henle's loop

- The ascending thick limb of Henle's loop is 9 to 10 mm in length and 30 to 40 μm in diameter. It joins the ascending thin limb of Henle's loop at the junction of the inner stripe with the inner zone of the medulla and ascends straight up through the medulla to reach the cortex.
- The low cuboidal epithelial cells, interdigitating with each other.
- Basal interdigitations are much more mitochondria of the proximal convoluted tubules, and form highly efficient zonulae occludentes with their neighboring cells.

Distal tubule



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Pars recta / Ascending thick limb of Henle's loop (cont.)

- The thick ascending limb is impermeable to water or urea.
- Its cells have chloride (and perhaps sodium) pumps that function in the active transport of chloride (and sodium) from the lumen of the tubule.
- Thus, as the filtrate reaches the cortex of the kidney within the lumen of the distal tubule, its salt concentration is low and its urea concentration remains high.
- These cells also symthesize Tamm-Horsfall protein, which they release into the lumen of the thick ascending limb to impede the formation of kidney stones.

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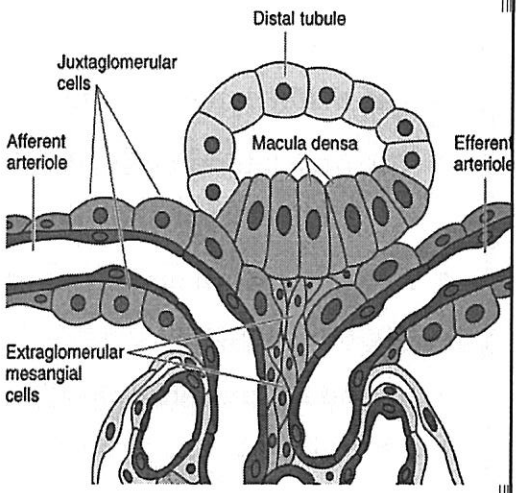
Pars recta / Ascending thick limb of Henle's loop (cont.)

- As the ascending thick limb of the Henle loop passes near its own renal corpuscle, it lies between the afferent and efferent glomerular arterioles.
- This region of the distal tubule is called the macula densa.
- Because the cells of the macula densa are tall and narrow, the nuclei of these cells appear to be much closer together than those of the remainder of the distal tubule.



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Pars convoluta / Distal convoluted tubule

- Distal convoluted tubules are short (4 to 5 mm) with an overall diameter of 25 to 45 μm.
- The lumens are wide-open, the low cuboidal lining epithelium is polar than that of proximal convoluted tubules.
- The cells are narrower with a few, blunt apical microvilli, round & apically located nuclei, one or two dense nucleoli and numerous mitochondria.
- Basal interdigitations are not as extensive as those of the ascending thick limb of Henle's loop.

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Pars convoluta / Distal convoluted tubule (cont.)

- Ascending tubule drain into the arched portion of the collecting tubules.
- The distal convoluted tubule is impermeable to water and urea.
- The basolateral plasmalemma of its cells has high Na^+,K^+-ATPase, in response to the hormone aldosterone.
- Actively resorb almost all of the remaining Na^+ and passively Cl^- from the lumen of the tubule into the renal interstitium.
- K^+ and H^+ ions are actively secreted into the lumen, thus controlling the body's extracellular fluid potassium level and the acidity of urine, respectively.

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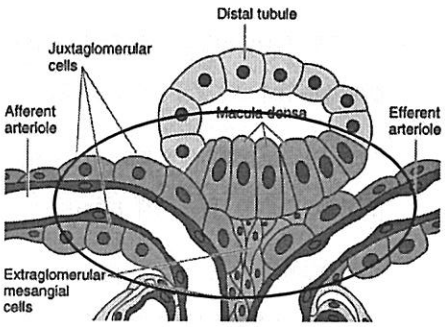
Juxtaglomerular Apparatus

- Juxtaglomerular apparatus consists of
  1. Macula densa of the distal tubule,
  2. Juxtaglomerular cells of the adjacent afferent (occasionally, efferent) glomerular arteriole, and
  3. Extraglomerular mesangial cells (also known as polkissen, lacis cells, and polar cushion).
- Absent basal lamina between Juxtaglomerular cells and the cells of the macula densa, permitting intimate contact between cells.



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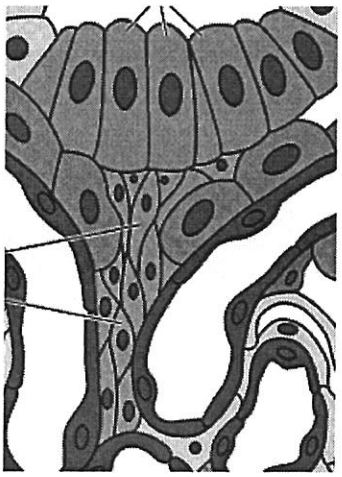
Juxtaglomerular Apparatus (cont.)

1. Macula densa cells are tall, narrow, pale with centrally placed nuclei, appear as a dense spot.

2. Juxtaglomerular cells are the modified smooth muscle cells located in the tunica media of afferent glomerular arterioles, richly innervated by sympathetic nerve fibers.

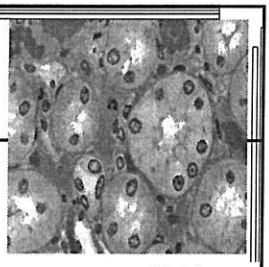
   ♣ Juxtaglomerular cells contain specific granules demonstrated to be the proteolytic enzyme, renin, Angiotensin-converting enzyme (ACE), angiotensin I, and angiotensin II.

3. Extraglomerular mesangial cells occupy the space bounded by the afferent arteriole, macula densa, efferent arteriole, and vascular pole of the renal corpuscle.



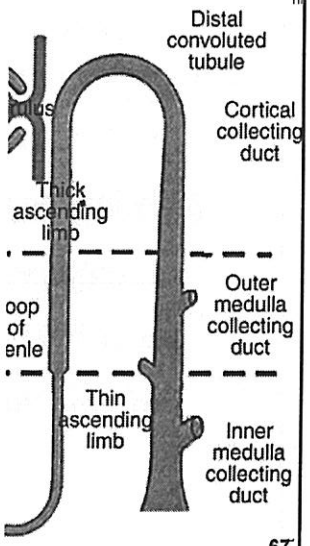
✖ These cells may contain occasional granules and are probably contiguous with the intraglomerular mesangial cells.

5. Collecting tubules



- The distal convoluted tubules of several nephrons join to form a short connecting tubule that leads into the collecting tubule.
- Ultrafiltrate that enters the collecting tubule is modified and delivered to the medullary papillae.
- Collecting tubules are about 20 mm long and have three recognized regions:

  1. Cortical 2. Medullary 3. Papillary



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Cortical collecting tubules

- Cortical collecting tubules are located in the medullary rays and are composed of two types of cuboidal cells:
  - Principal cells
  - Intercalated cells

Principal cells have oval, centrally located nuclei, a few small mitochondria, and short, sparse microvilli.

The basal membranes of these cells display numerous infoldings.

- These cells possess numerous aquaporin-2 channels that are very sensitive to antidiuretic hormone (ADH) and become completely permeable to water.

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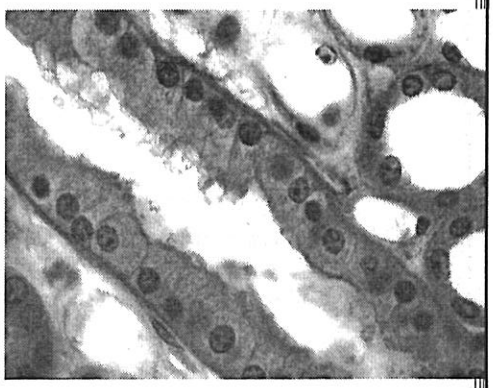
Intercalated cells display numerous apical vesicles 50 to 200 nm in diameter and an abundance of mitochondria, round & centrally located nuclei.

- There are two types of intercalated cells:
  - Type A, whose luminal membrane possesses H^+-ATPase that functions in transporting H^+ into the lumen of the tubule thus acidifying urine; and
  - Type B, whose basolateral membrane possesses H^+-ATPase and functions in resorbing H^+ and secreting HCO^{3-}.

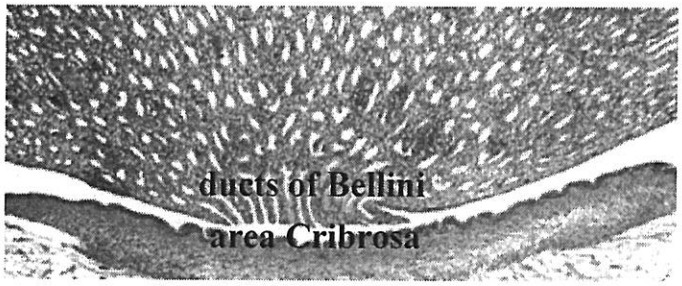
Medullary collecting tubules

- Medullary collecting tubules are of larger caliber because they are formed by the union of several cortical collecting tubules.
- In the outer zone of the medulla are similar to the cortical collecting tubules in that they display both principal and intercalated cells.
- In the inner zone of the medulla have principal cells only.



Papillary collecting tubules (ducts of Bellini)

- Papillary collecting tubules (ducts of Bellini) are each formed by the confluence of several medullary collecting tubules.
- These are large ducts, 200 to 300 μm in diameter, and they open at the area cribrosa of the renal papilla to deliver the urine that they convey into the minor calyx of the kidney.
- These ducts are lined by tall columnar principal cells only.



Renal Interstitium

- At the hilum, a thin connective tissue cover, some of which is derived from the capsule.

1. Cortical interstitium has two cellular components fibroblasts and dendritic cells.
2. Medullar interstitium consists of three cell types of Fibroblasts, Macrophages and Interstitial cells.

- Interstitial cell is believed that these cells synthesize
  - Prostaglandins : vasoconstrictor / hypertension
  - Prostacyclin : prevent platelet formation and clumping in blood clotting. It is also an effective vasodilator
  - Medullipin I; is converted in the liver to medullipin II, potent vasodilators that lowers blood pressure / antihypertension in kidney.

Renal Circulation

Arterial supply

- Renal artery bifurcates into an anterior and a posterior division --> enter hilum ----> subdivide to 5 Segmental arteries ----> Lobar artery for each lobe ----> 2-3 Interlobar arteries between renal pyramids ----> Arcuate arteries at corticomedullary junction ----> Interlobular arteries within cortical labyrinth ----> branch into Afferent glomerular arterioles to supply the glomeruli of the renal corpuscles ----> drain to Efferent glomerular arterioles ----> Peritubular capillaries ----> Vasa recta ----> Venae rectae ---->Renal vein

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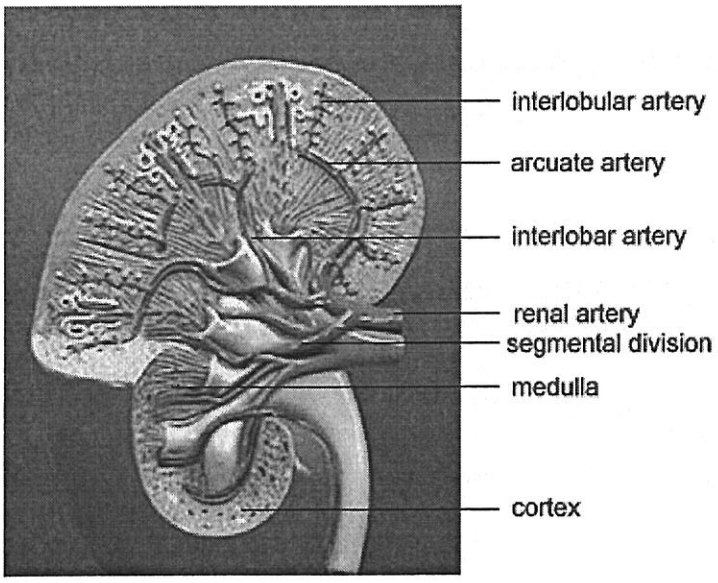
Arteral Supply



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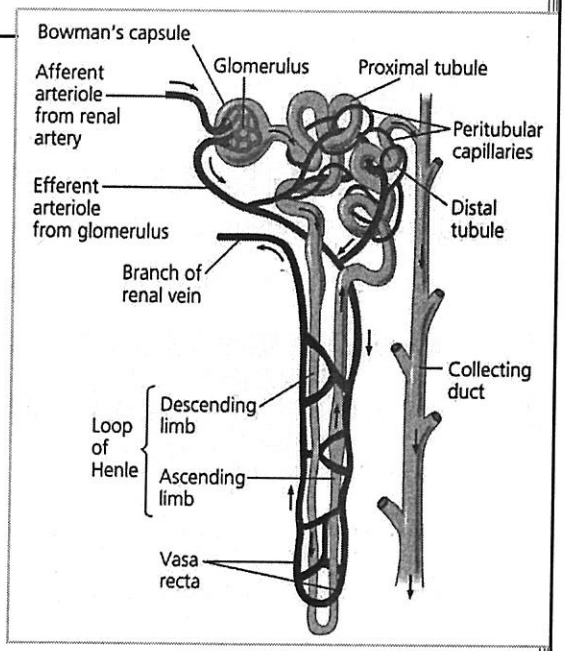
Venous Drainage

Venae rectae ----> Arcuate veins ----> Stellate veins ----> Interlobular veins ----> Interlobar veins ----> Renal vein



Renal Innervation

- Most nerve fibers are unmyelinated, sympathetic fibers that form the renal plexus, traveling along the renal artery.
- Sympathetic fibers reach the epithelium of the renal tubules, the juxtaglomerular and interstitial cells, and the capsule of the kidney.

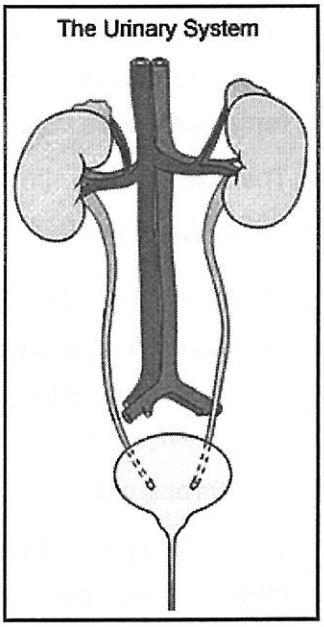
Excretory Passages

Calyx

Ureter

Urinary Bladder

Urethra



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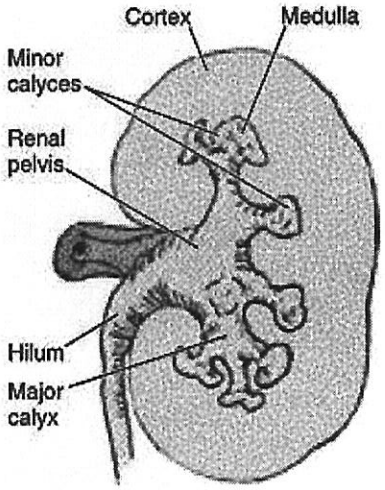
Calyx

- Renal papilla of each renal pyramid fits into a minor calyx, a funnel-shaped chamber that accepts urine leaving the ducts of Bellini at the area cribrosa.
- Minor calyx is covered by transitional epithelium.
- Deep to the lamina propria is a thin smooth muscular layer to propels the urine into a major calyx.



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Ureter

- Each ureter is about 3 to 4 mm in diameter, is approximately 25 to 30 cm long, and pierces the base of the urinary bladder.
- The ureters are hollow tubes consisting of:
  - Mucosa: transitional epithelial lining
  - Lamina propria:
  - Muscularis: outer circular and inner longitudinal
    - lower one third of the ureter: outer longitudinal, middle circular, and inner longitudinal.
  - Fibrous outer coat
- The ureters pierce the posterior base of the bladder, a valve-like flap of mucosa hangs over ureteric orifice, preventing regurgitation of urine from the bladder back into the ureters.

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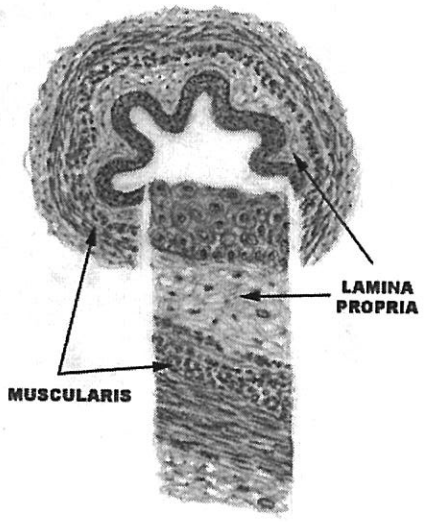
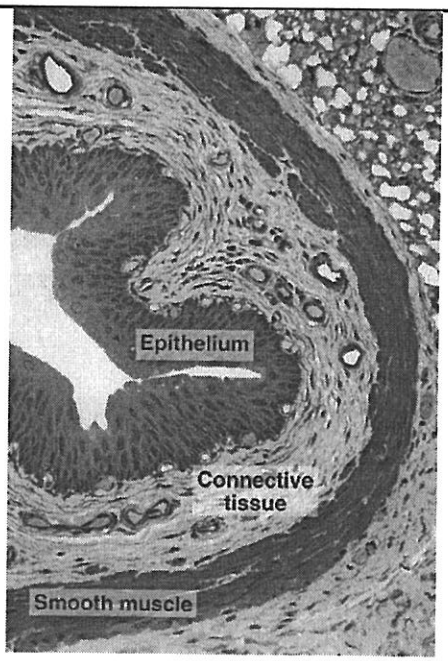
Ureter





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Urinary Bladder

- **The urinary bladder is essentially an organ for storing urine until the pressure becomes sufficient to induce the urge for micturition, or voiding. It is composed of 4 layers:**
  - **Mucosa also acts as an osmotic barrier between the urine and the lamina propria and is arranged in numerous folds, which disappear when the bladder becomes distended with urine.**
  - **Lamuna propria**
  - **Muscularis: inner longitudinal layer (thin), middle circular layer (thick) and outer longitudinal layer (thin)**
    - **middle circular layer forms the** internal sphincter muscle **around the internal orifice of the urethra.**
  - **Adventitia**

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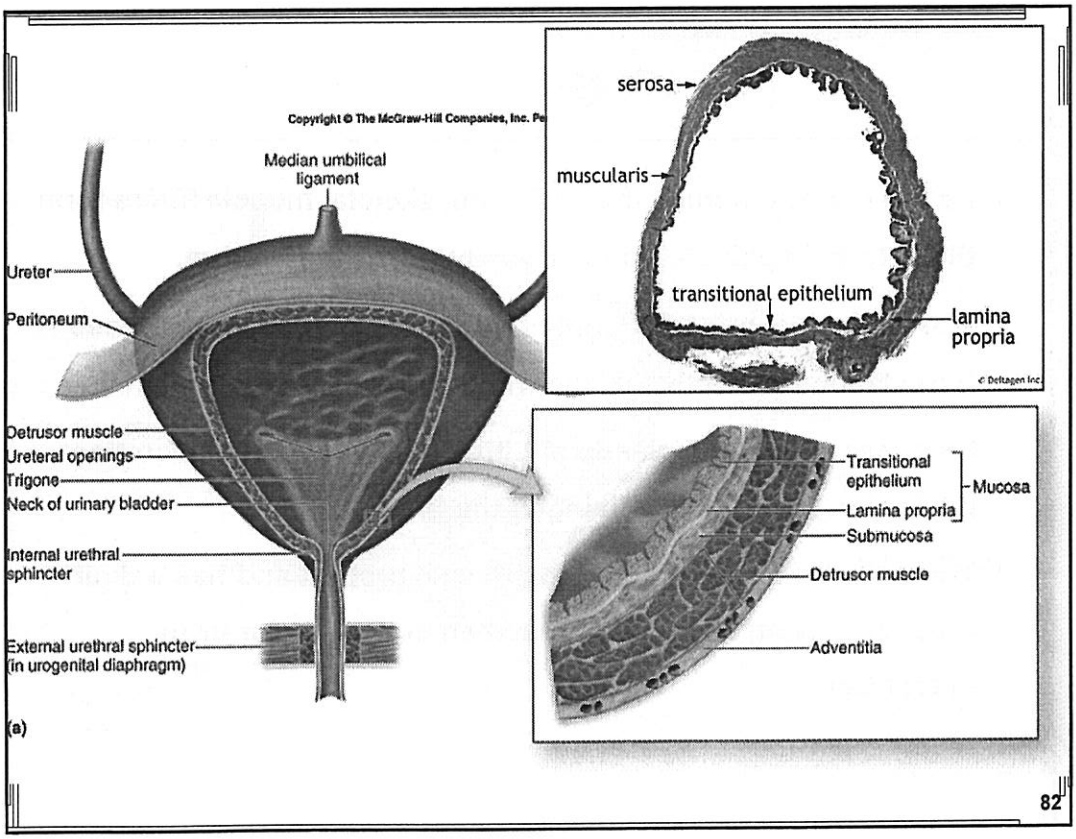

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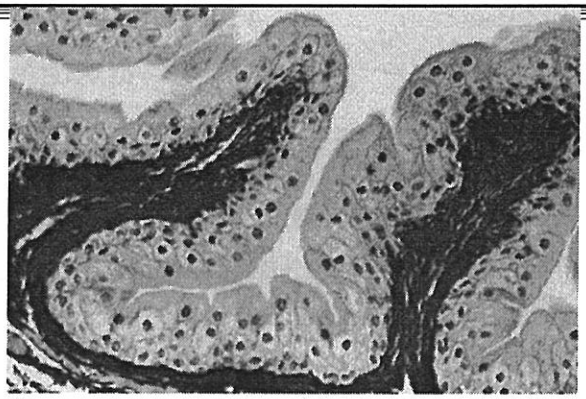
Empty Bladder



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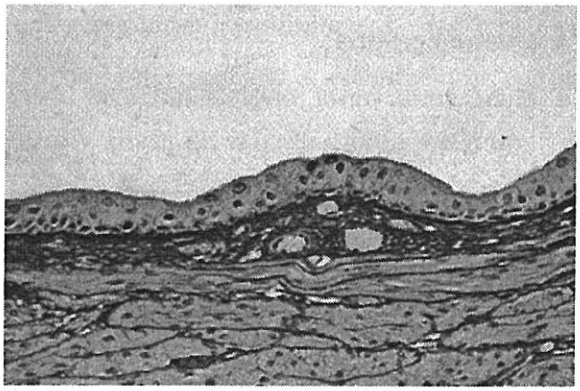
Full Bladder



B

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Urethra

- As the urethra pierces the perineum, skeletal muscle fibers form the external sphincter muscle surrounding the urethra.
- The lamina propria of all three regions is composed of a loose fibroelastic connective tissue with a rich vascular supply.
- It houses numerous glands of Littre, whose mucous secretion lubricates the epithelial lining of the urethra.
- The male urethra is longer than female urethra and has a dual function, acting as a route for semen as well as for urine micturition.

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Female Urethra

- The female urethra is about 4 to 5 cm in length and 5 to 6 mm in diameter.
- Urethral orifice opens to the vagina.
- It is lined by a transitional epithelium near the bladder and by a stratified squamous nonkeratinized epithelium along the remainder of its length.
- Interspersed in the epithelium are patches of pseudostratified columnar epithelium.

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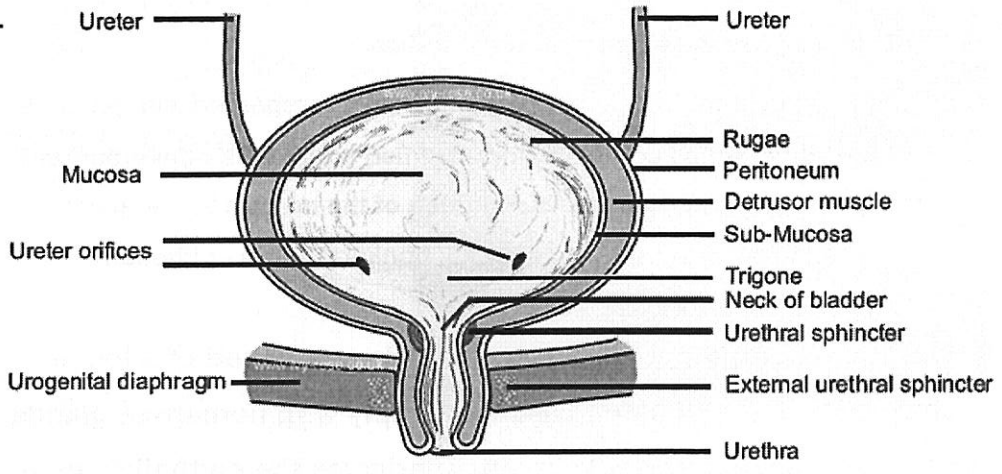
Female Excretory Passage



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Male Urethra

- The male urethra is 15 to 20 cm long, and its three regions:

  1. Prostatic urethra, 3 - 4 cm long, lies entirely in the prostate gland.

     It is lined by a transitional epithelium and receives the openings of many tiny ducts of the prostate, the prostatic utricle and the paired ejaculatory ducts.

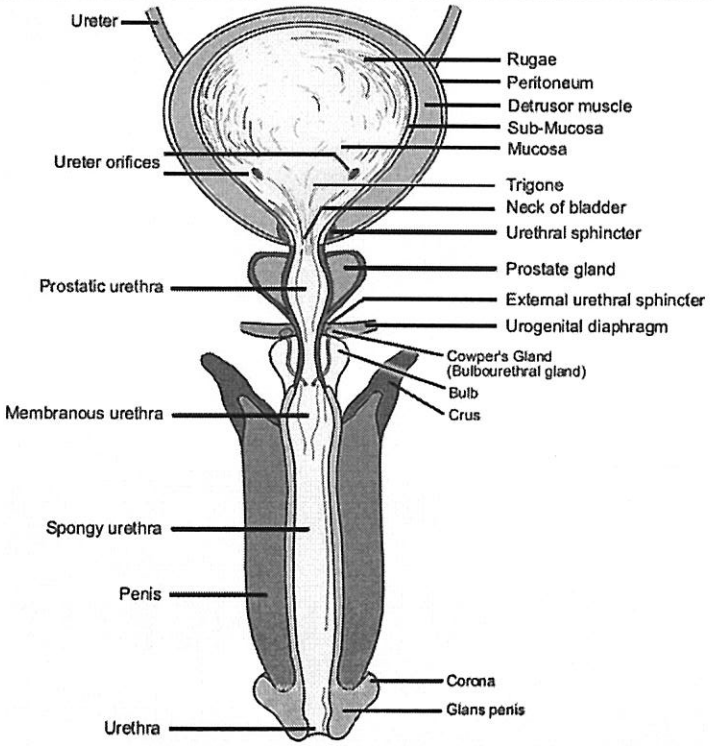
  2. Membranous urethra is only 1 - 2 cm long, passes through the perineal membrane. It is lined by stratified columnar epithelium interspersed with patches of pseudostratified columnar epithelium.

  3. Spongy urethra (penile urethra), the longest portion of the urethra, passes through the length of the penis, terminating at the tip of the glans penis as the external urethral orifice.

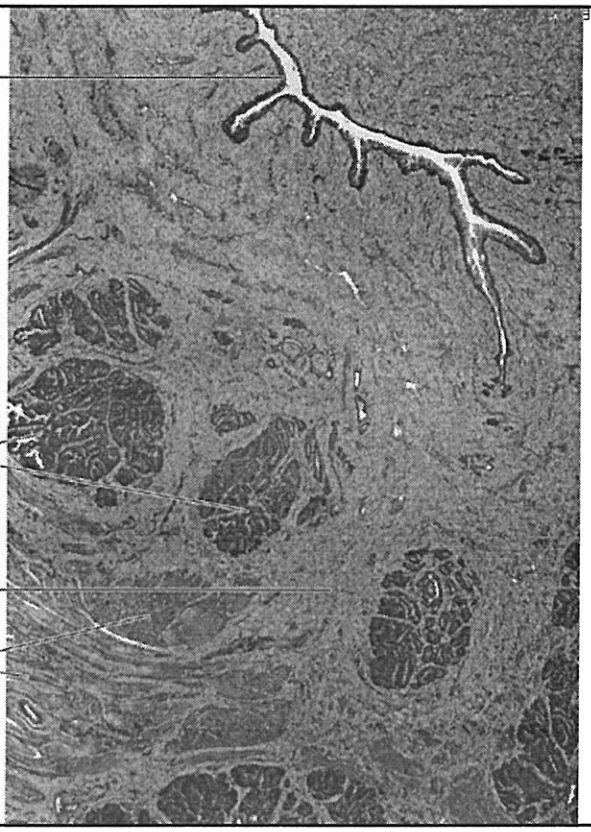
     It is lined by stratified columnar epithelium interspersed with patches of pseudostratified columnar and stratified squamous nonkeratinized epithelia. The enlarged terminal portion of the urethra in the glans penis is lined by stratified squamous nonkeratinized epithelium.

- The lamina propria of all three regions is composed of a loose fibroelastic CT with a rich vascular supply with numerous glands of Littre, whose mucous secretion lubricates the epithelial lining of the urethra.

Male Excretory Passage



Male Urethra



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