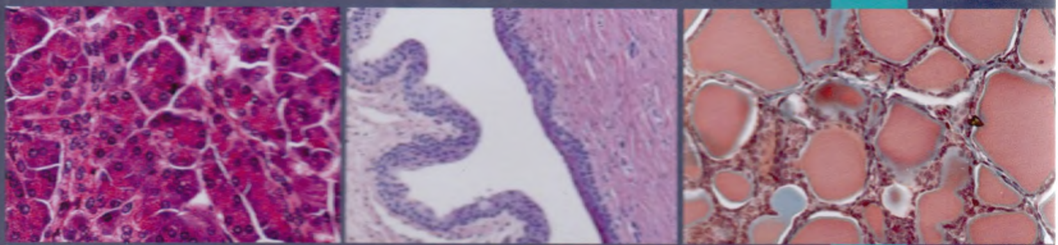
Fiadotau D. N., Yunusov Kh. B.

VETERINARY HISTOLOGY

Textbook



Publishing house
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*Samarkand Institute of Veterinary Medicine,
Animal Husbandry and Biotechnology*

Vitebsk State Academy of Veterinary Medicine

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Veterinary Histology is a microscopic anatomy textbook focused on domestic species. This textbook provides comprehensive, system-specific text as well as high-resolution, annotated images along.

Organized by body system, this resource provides coverage of the structure and function of the organs of a range of domestic animal species. Bridging the gap between the physiology and the gross anatomy of organisms, it also explores discoveries made in the areas of molecular biology.

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Reviewers: Jukov A.I.

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CONTENTS

STOMACH

The stomach is a key part of the gastrointestinal (GI) tract, sitting between the esophagus and duodenum. Its functions are to mix food with stomach acid and break food down into smaller particles using chemical and mechanical digestion.

The stomach can perform these roles due to the layers of the stomach wall. These are the gastric mucosa, submucosa, muscularis externa and serosa. All parts of the GI tract tend to follow this same pattern of tissue layer arrangement, which means that the stomach is essentially just a widening of the GI tube.

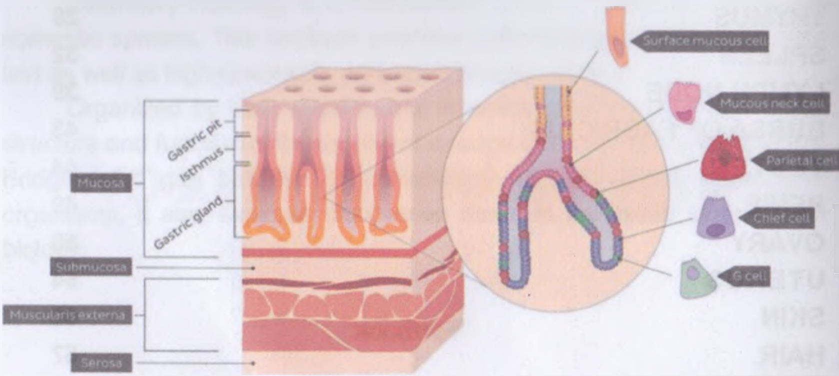

Fig. 1. Gastric gland and gastric wall: histology diagram

The stomach wall consists of 4 layers of tissue. From deep (external) to superficial (internal) these are the serosa, muscularis externa, submucosa and mucosa. This layered arrangement follows the same general structure in all regions of the stomach, and throughout the entire gastrointestinal tract. The outer layer of the stomach wall is smooth, continuous with the parietal periotenum. The inner wall (mucosa and submucosa layers) is thrown into folds known as rugae, or gastric folds, which allow the stomach to distend upon the entry of the food. A bolus of food enters the stomach from the esophagus. The various tissue layers of the stomach wall then [illegible] functions to digest the bolus into a viscous, pulpy fluid called chyme. Chyme is directed into the duodenum of the small intestine for further digestion and absorption.

Layers of the stomach wall	
Mucosa	*Surface mucous cells:* simple columnar epithelium *Gastric pits:* surface mucous cells *Gastric glands:* parietal, chief, enteroendocrine cells *Lamina propria:* connective tissue *Muscularis mucosa:* two smooth muscle layers
Submucosa	Connective tissue, submucosal (Meissner's) plexus
Muscularis externa	Smooth muscle layers (longitudinal, circular, oblique), myenteric (Auerbach's) plexus
Serosa	Connective tissue, mesoderm

All 3 types of glands are long, branched, tubular structures, extending through the whole thickness of the lamina propria. However, their cellular composition differs based on their location and associated function. Gastric glands proper is very rich in digestive enzyme producing parietal and chief cells, as the majority of digestion takes place in the body and fundus of the stomach. Pyloric and cardiac glands largely lack parietal and chief cells but have abundant mucous neck cells. This makes sense, as these segments are areas of transition between the stomach and other parts of the GI tract. Therefore, the mucous secretions they produce protect the oesophagus and the duodenum from the corrosive effects of the gastric juices. Enteroendocrine cells are scattered throughout all types of gastric glands.

The epithelium of the villi is made up of tall columnar absorptive cells called enterocytes, and goblet cells, which secrete mucin, for lubrication of the intestinal contents, and protection of the epithelium.

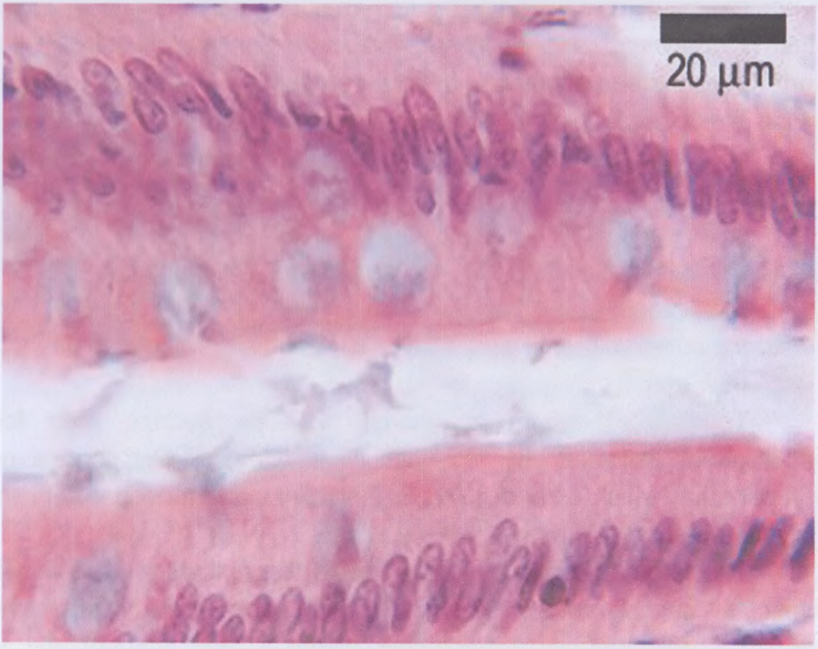

Fig. 3. The epithelium

This shows the epithelium of part of a villus at high magnification. You should be able to identify goblet cells, and enterocytes, and notice the «brush border» on the apical surface of the enterocytes, which is due to the microvilli.

The crypts additionally contain

- Paneth cells (at the base of the crypts) - they have a defensive function, and stain intensely eosinophilic, due to secretory granules of antimicrobial peptides called defensins, as well as lysozyme and phospholipase A. These cells last for several weeks.

- Endocrine cells, (also eosinophilic) which produce secretin, somatostatin, enteroglucagon and serotonin. One type of endocrine cell for each type of hormone.
- Stem cells, found at the base of the crypts, which divide continuously to replace enterocytes (every 2-3 days), goblet cells, paneth cells and neuroendocrine cells. Intraepithelial lymphocytes (mostly T-cells).

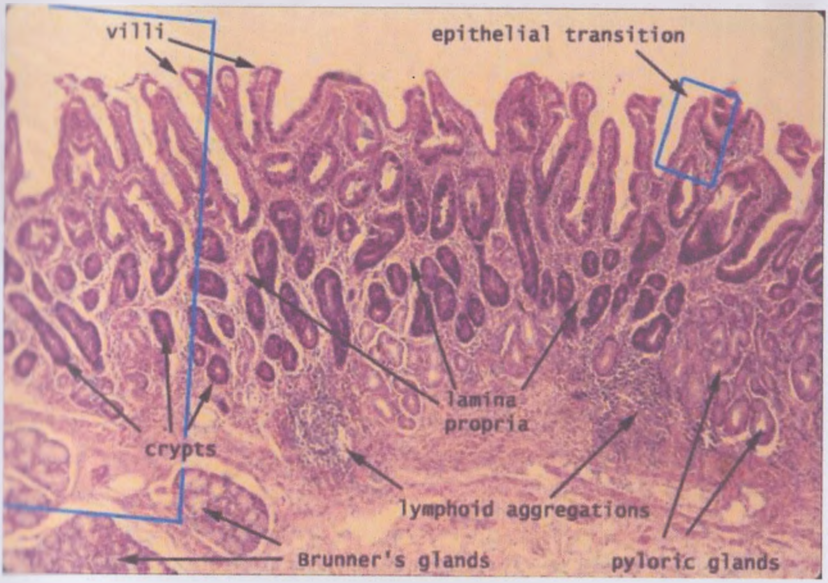

Fig. 4. Small Intestine

Look at this picture of a section through the duodenum. Identify villi, crypts, muscularis mucosae, mucosa, muscularis externa and Brunner's glands.

The first part of the small intestine is the duodenum, and its structure is similar to that seen elsewhere in the small intestine, with some differences. The villi are broader, Peyers Patches are less common, and it has one unique feature: Brunner's glands, which are found in the sub-mucosa.

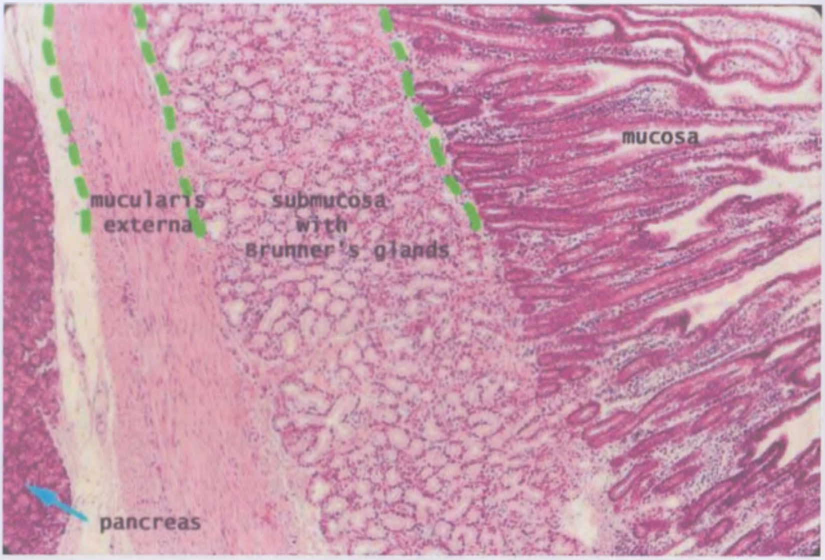

Fig. 5. Duodenum

The duodenum is often mistaken for the small intestine, so take a moment to compare this section to that of the small intestine in the picture above. Make sure you can distinguish correctly between the two and identify Brunner's glands correctly.

Both Brunner's glands, and the goblet cells in the duodenum secrete mucus. The mucus secreted by Brunner's glands is alkaline and helps to neutralise the acid chyme produced by the stomach, to produce chyme with a pH suitable for the digestive enzymes of the small intestine.

LARGE INTESTINE

The large intestine consists of the cecum, colon, rectum, and anal canal. The colon is mainly responsible for reabsorbing water and electrolytes from the feces within its lumen. The colon is continuous with the rectum, where the feces is stored before defecation. Similar to the rest of the large intestine, the colon has 4 main layers: the mucosa, submucosa, muscularis propria, and a surrounding serosal layer of connective tissue that isn't seen in this image.

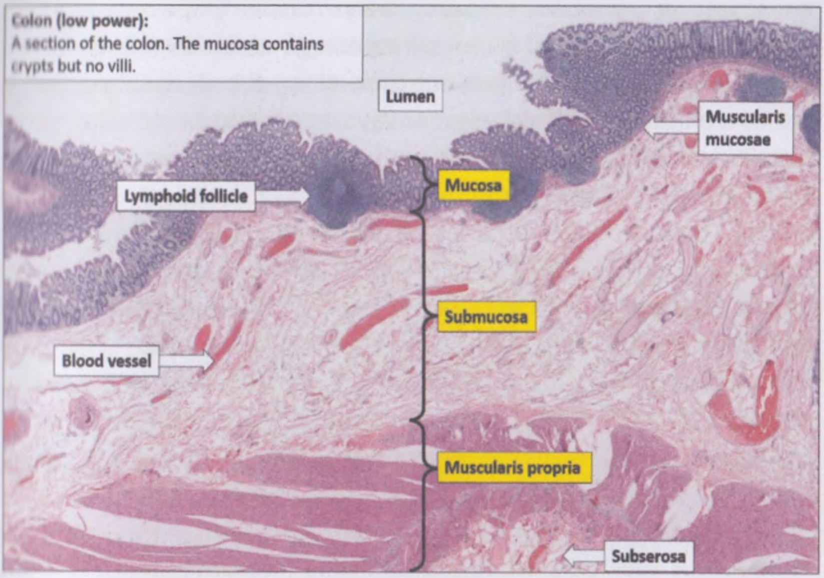

Fig. 6. Colon

Even at low magnification, we can see that the colon's mucosa at the top of this image does not have the distinct long villi or finger-like projections that would normally be seen in the small intestine. Taking a closer look at the colon's mucosa, the lumen of the colon is seen at the top of the image and the first layer of cells lining the mucosa is the epithelium of the mucosa. The epithelium consists of two types of cells, enterocytes, and goblet cells. The enterocytes or absorptive cells are the simple columnar cells with microvilli. They are also called the absorptive cells because of their main function of absorbing water from the colon lumen. And the goblet cells are responsible for secreting mucus. Although the cells are not clearly seen in this image, the mucus they produce is easily seen as the globular structures that are stained dark purple from the hematoxylin and eosin stain.

The surface epithelium is continuous with straight, unbranched, tubular glands called the crypts of lieberkühn. Unlike the crypts in the small intestine, these crypts extend through the majority of the mucosa, from their openings at the intestinal surface all the way to the muscularis mucosa along the deepest portion of the overall mucosa. It may not always appear to be continuous on histological slides because the path of the crypts may not always travel along the same plane as the section of tissue taken from the colon. The superficial portions of the crypts will typically have a higher concentration of enterocytes and the deeper portions will have a high concentration of goblet cells. The tissue found between the crypts and the epithelium is the lamina propria, which consists of many types of immune cells, including plasma cells, lymphocytes, eosinophils, and macrophages. And finally, the deepest layer of the mucosa is a thin layer of smooth muscle called the muscularis mucosa.

Beneath the mucosa is the next major layer of the colon, the submucosa. This layer consists mostly of dense irregular connective tissue, but also contains blood vessels, lymphatic vessels, and the submucosal or meissner's plexus. Meissner's plexus is a network of nerves that innervate the goblet cells in the mucosa as well as the smooth muscle of the muscularis mucosa. In this image, there is a relatively large cross-section of a bundle of nerve cells that are part of meissner's plexus. We can also see a number of large blood vessels and a lymphatic vessel in the upper left of this image.

LIVER

The liver consists of the following major histological components:

1. Parenchyma, which is represented by hepatocytes.
2. Stroma, which is a continuation of the surrounding capsule of Glisson. It consists of connective tissue and contains the vessels. The capsule is also covered by a layer of mesothelium, arising from the peritoneum covering the liver. The connective tissue of the stroma is type III collagen (reticulin), which forms a meshwork that provides integrity for the hepatocytes and sinusoids.
3. Sinusoids, which are capillaries travelling between hepatocytes
4. Spaces of Disse (perisinusoidal spaces), which are located between the hepatocytes and the sinusoids.

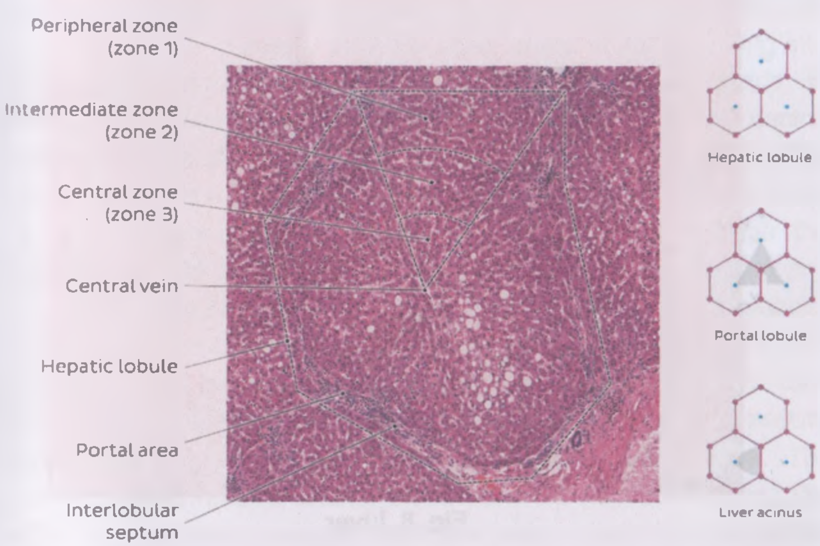

Fig. 7. Liver histology

In histological terms, the liver consists of a large number of microscopic functional units that work in unison to ensure the overall, proper activity of the entire organ. There are three possible ways of describing one such unit, as given below:

- Hepatic (classic) lobule
- Portal lobule
- Liver acinus

The classic lobule is the traditional description and the one that you have most likely heard of the most. It consists of hexagonal plates of hepatocytes stacked on top of each other. Within each plate, the hepatocytes radiate outwards from a central vein. As they extend towards the periphery, the hepatocytes are arranged into strips, similar to the spokes of a cartwheel. Hepatic sinusoids travel between the strips of hepatocytes, draining into the central vein.

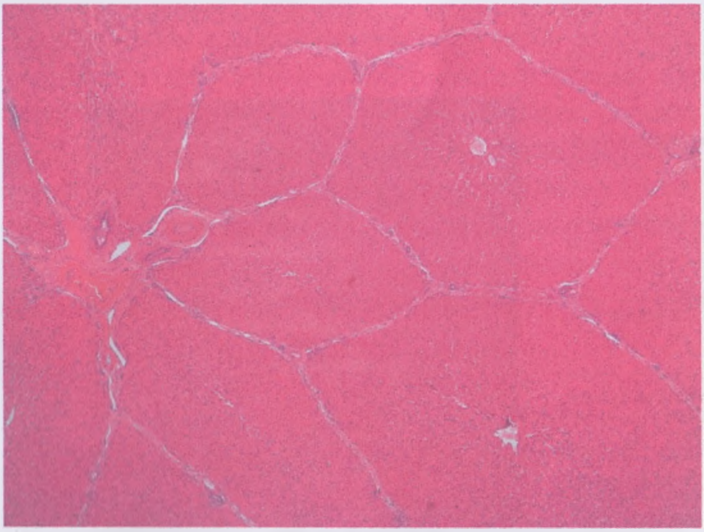

Fig. 8. Liver

One portal canal is located at each corner of the hexagonal classic lobule, making a total of six for each lobule. These portal canals are composed of the portal triads, which are surrounded by loose stromal connective tissue. A periportal space (space of Mall), where lymph is produced, is sandwiched between the connective tissue of the portal canals and the hepatocytes.

While connective tissue is present around the portal canals, the interlobular quantity is very small in humans. This can make routine histological visualizations of the classic lobule difficult. These large and polyhedral (six surfaces) cells make up 80% of the total cells of the liver. They can contain between two and four nuclei, which are large and spherical, occupying the centre of the cells. Each nucleus has at least two nucleoli. The typical lifespan of a hepatocyte is five months. The adjacent hepatocytes leave a very small space between them known as bile canaliculi which are almost 1.0-2.0 μm in diameter. The cell membranes near these canaliculi are joined by tight junctions.

The name of the blood vessels travelling through the portal canals are called interlobular vessels. They send blood into the sinusoids, either directly if they are really small, or by branching into distributing vessels first, which in turn empty into the sinusoids via inlet vessels. From the sinusoids, the blood drains into the central vein, which occupies the central axis of the classic liver lobule. The endothelial cells forming the central veins are surrounded by a small quantity of connective tissue fibers. As they travel through the parenchyma, the central veins become larger, subsequently emptying into the sublobular veins. The endothelial lining of the sublobular veins is surrounded by a high quantity of connective tissue fibers, consisting of a layer of both collagenous and elastic fibers. Several sublobular veins then converge into larger and valveless hepatic veins, which ultimately empty into the inferior vena cava. The sinusoids also receive arterial blood from the hepatic arteries. The latter have a thick muscular wall and also supply the connective tissue and various structures in the portal canals. In addition, sinusoids contain a specific cell type called Kupffer cell, containing ovoid nuclei.

PANCREAS

Examine slide at the lowest power and note that most of the section appears purple or bluish. This is the parenchyma (or functional tissue) of the exocrine pancreas. You will note that the parenchyma is rather indistinctly divided into smaller areas by slits of open space or by pink connective tissue (stroma). The smallest of these areas constitute the lobules of this gland. You may see a few circular structures of various size between the lobules. These are cross sections either through branches of the pancreatic duct or through blood vessels. If you observe the parenchyma carefully you will note scattered small spots that are a lighter blue gray. These are the islets of Langerhans, which comprise the endocrine pancreas.

First observe the parenchyma, noting that it is made up of large numbers of acini, although you may also see occasional fat cells in the parenchyma. Each acinus is a cluster of secretory cells arranged around a small lumen (which is generally collapsed and therefore not visible in your sections). The acini may vary considerably in shape since they are cut randomly in the section. Note that the peripheral region of each acinus, which represents the basal portions of the individual acinar cells, stains more blue or purple. The hematoxylin component of the H&E stain is staining the ribosomal RNA in the abundant rough (or granular) endoplasmic reticulum found in this portion of the secretory cells.

This «cytoplasmic basophilia» is the reason why the whole section appears purple or blue. The central region of the acinus, representing the apical portions of the acinar cells, is pink (acidophilic) because of the presence of the Golgi complex and numerous secretory granules in this part of the cell (you will probably not be able to make out the individual granules). Here and there you may see a smaller cell, or cluster of cells, with pale cytoplasm in the central region of an acinus. These are centroacinar cells and represents the initial portion of the excurrent duct that extends up into the acinus. These slender ducts extending from the acini to larger excretory ducts located outside the lobule are called intercalated ducts and may be found by looking for small clusters of 3-5 slightly elongated nuclei lying between the acini; the cytoplasm of the duct cells is very pale, and you may or not be able to make out the lumen. As in salivary glands, intercalated ductal cells in the pancreas contribute bicarbonate ions (sodium and water follow passively) to the exocrine secretory product. However, unlike salivary glands, there are no striated ducts in the pancreas to recover sodium, so the final product is rich in both sodium and bicarbonate (as opposed to saliva in which the sodium content is about one tenth that of plasma).

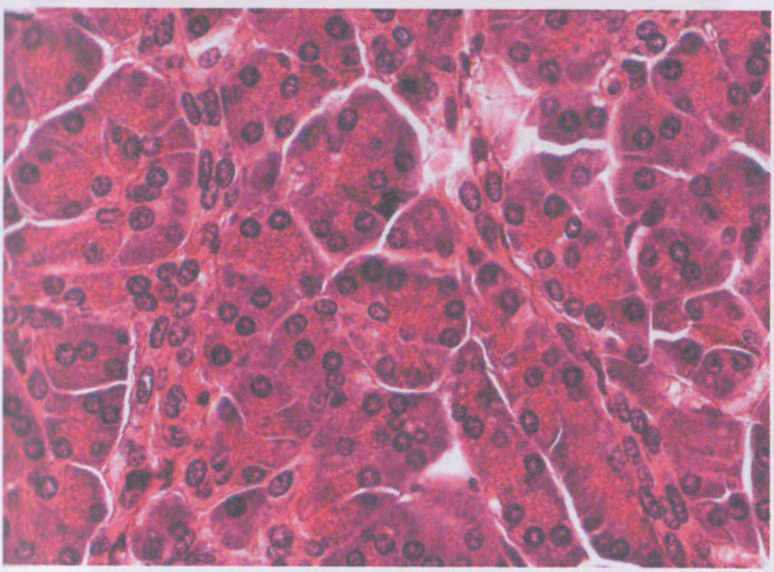

Fig. 9. Pancreas

Using intermediate or low power, observe the larger ducts that are located in the connective tissue septa between the lobules. These interlobular ducts slide can be distinguished from blood vessels by their lining epithelium, which is either simple cuboidal or, in the larger ducts, simple columnar.

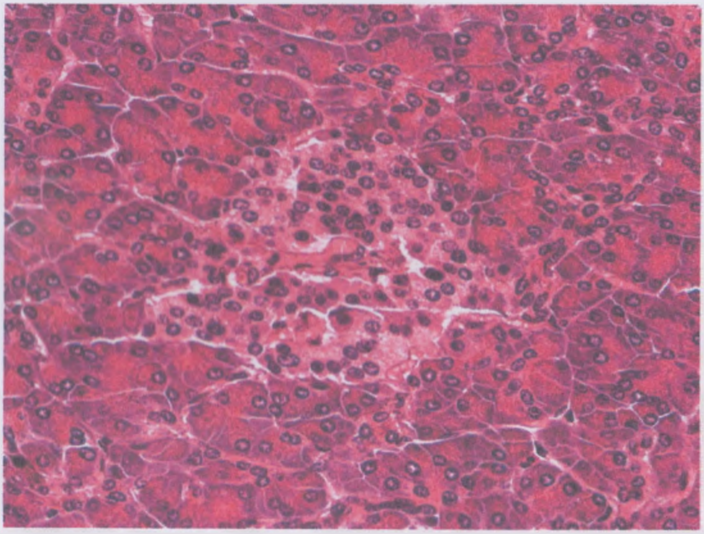

Fig. 10. Islets of Langerhans

Scan the parenchyma of this slide to find islets. The staining procedure used here allows you to differentiate the two principal cell types found in the islets. Although the nuclei in both a and b cells are reddish, the insulin secretory granules in the beta (or B) cells cause the cytoplasm to stain a pale blue green with the chrome-alum hematoxylin. The alpha (or A) cells, containing secretory granules of glucagon, are stained reddish. Note that the beta cells are usually more numerous and occur in the interior of the islet, while the alpha cells are found more peripherally. You will not be able to distinguish delta (or D) cells, source of somatostatin. Incidentally, the secretory granules of the acinar cells are seen clearly in the exocrine pancreas in this slide. Islets of Langerhans can also be readily seen in slide Islets of Langerhans as well. The islets occur as pale areas of cells here and there in the parenchyma (you can find them most easily under low power). Note the scattered distribution of the islets and their variation in size. You will not be able to distinguish the various cell types in the islets in this routine H&E preparation.

PITUITARY GLAND

These slides show mostly pars distalis, but also have a small area of neurohypophysis (either pars nervosa or infundibular stalk) on one side (see slide orientation diagrams) and are stained in alternate sets with H&E or with Masson trichrome. The two classes of anterior pituitary cells (acidophils and basophils) are most easily distinguished with Masson trichrome staining, but you should also see how they look with routine H&E staining.

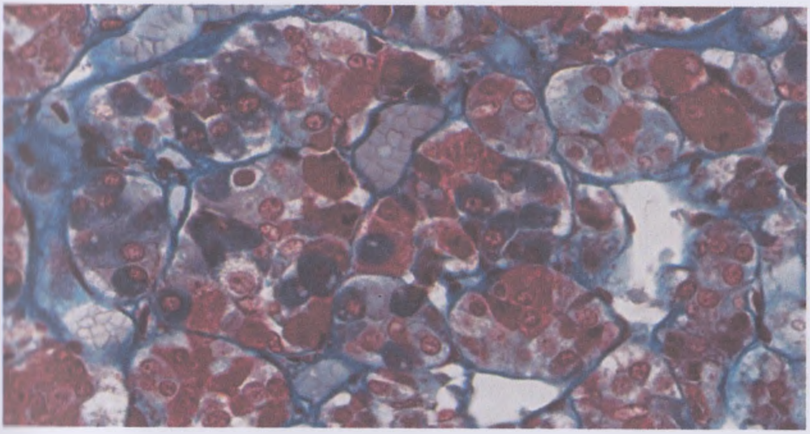

Fig. 11. Pituitary Gland

Study the pars distalis (anterior lobe) in the slide stained with Masson trichrome pars distalis. The cells are arranged in irregular clusters or cords and are distinguishable by their staining as either acidophils, basophils, or chromophobes. The acidophils stain red or orange-red, while the basophils stain various shades of blue or blue gray.

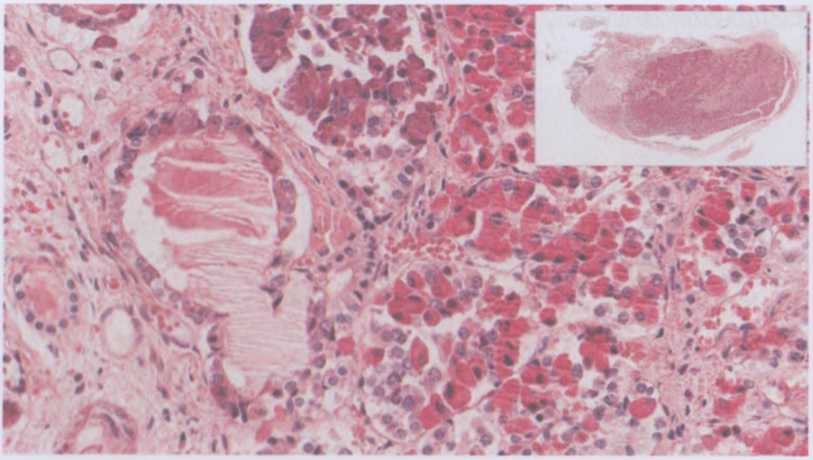

Fig. 12. Pituitary Gland

Remember that the acidophils include two different cell types, somatotropes (growth hormone) and mammotropes (prolactin), while the basophils include gonadotropes (FSH and LH), thyrotropes (TSH) and corticotropes (ACTH). ACTH is actually a cleavage product of pro-opiomelanocortin (POMC), which is made by corticotropes and processed primarily into ACTH in these cells. To a lesser extent, corticotropes also produce other signaling factors derived from POMC such as lipotropins (involved in lipid metabolism), endorphins (endogenous opioids that reduce pain perception), and melanocyte stimulating hormone (MSH). Occasional cells in the anterior pituitary show no distinctive staining and are called «chromophobes». You will only be required to distinguish acidophils from basophils. Your best strategy is first to identify acidophils, which are more distinctively stained, and then the remaining cells are almost entirely basophils. The cells are not uniformly distributed throughout the pars distalis, but instead there are areas where acidophils predominate, other areas where basophils are more numerous, while still other regions may show a more even mixture of acidophils and basophils. Note the abundant sinusoidal capillaries (often filled with red blood cells) sinusoidal capillaries that lie between the cell cords or clusters. You can appreciate how readily the hormones secreted from the cells can reach the blood.

Since collagen stains bright blue with the Masson trichrome method, you can see the delicate connective tissue partitions between cords and around blood vessels. In the routine H&E-stained sections, you can also identify acidophils and basophils, although the difference is not as obvious as it is with Masson trichrome staining. Here again, you should first identify acidophils, which stain various shades of reddish pink, and then the remaining cells are almost entirely basophils, which vary generally from bluish/grayish pink to blue.

THYROID GLAND

Examine slide at low magnification, then at higher magnifications. Note that the thyroid gland is made up of functional units called follicles, which in three dimensions are approximately spherical, their walls being composed of a simple cuboidal epithelium, surrounding a lumen that contains colloid. Note that the follicles vary in size and that the height of the follicular epithelial cells may also vary. The colloid is composed primarily of thyroglobulin, a glycoprotein synthesized by the follicular epithelium. Under stimulation from pituitary TSH, the thyroid cells break down the thyroglobulin to release thyroid hormones (T-3 and T-4), which pass into nearby capillaries. Occasional parafollicular cells (C-cells), source of the hormone calcitonin, are also present between the follicles and in the follicular epithelium. However, they are difficult to distinguish in routine histological slides of human thyroid, and you are NOT expected to recognize them based on light microscopy alone (but you should know that they are the source of calcitonin which is packaged into secretory granules that makes these cells readily identifiable by electron microscopy).

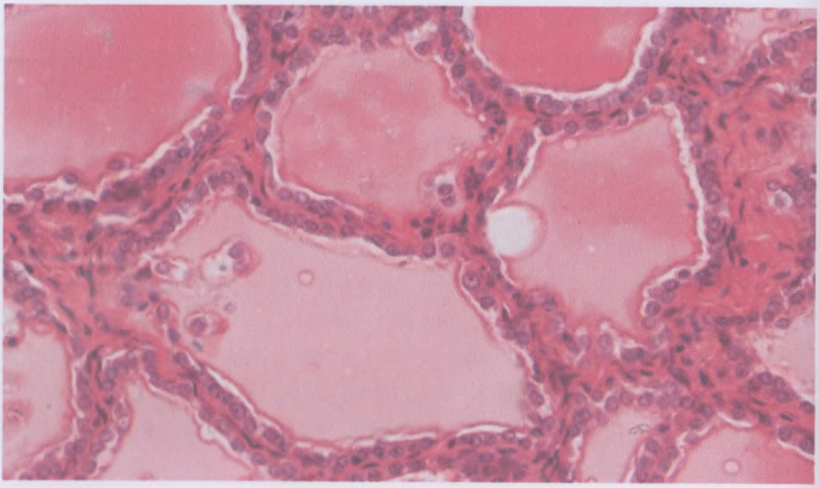

Fig. 13. Thyroid Gland

There are three versions of that show a rodent thyroid at three different levels of functional activity: normal, hypoactivity due to hypophysectom, and hyperactivity due to treatment with the drug thiouracil. Compare the tissue shown in each slide the variation is not overwhelming since the experiments were performed conservatively, but you should be able to see some differences in epithelial cell height and in the size of the follicular lumens. After hypophysectomy there is no stimulation by TSH, so the follicular epithelial cells become reduced in height and the colloid in the lumen is abundant, since it is not being resorbed to make thyroid hormones, C-cells are more obvious as these cells are fully functional and not dependent on TSH. In contrast, in the hyperactive follicles of thiouracil-treated animals the epithelium is columnar, and the follicular lumen is much reduced in size. The reason for this hyperactivity is that thiouracil blocks the oxidation of iodide, with the result that functional thyroid hormones can no longer be produced.

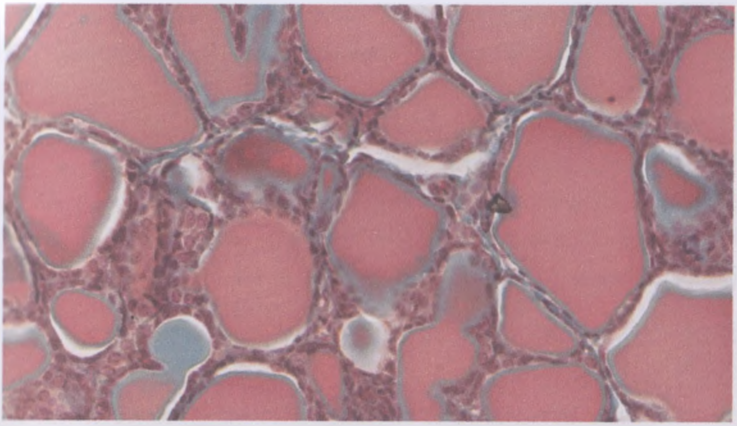

Fig. 14. Hypoactivity due to hypophysectom

The majority of the thyroid gland is made of spherical structures called follicles, instead of cords and clusters characteristic of the endocrine system. The central cavity of a follicle is filled with a colloid composed of **thyroglobulin**. Thyroglobulin is a glycoprotein that is a precursor and storage molecule for thyroid hormones. An extensive network of capillaries around follicles allows for the easy pick up of hormones by the blood.

The thyroid gland has two types of endocrine cells with different functions.

Follicular cells are the secretory (glandular) epithelial cells surrounding a cavity filled with a pink thyroglobulin. The height of the follicular cells reflects the functional state of the thyroid. The more active the cells, the taller the follicular cells. Follicular cells with normal activity are simple cuboidal; the highly active cells become columnar, the inactive cells flatten to squamous. Follicular cells produce and secrete the hormones thyroxine and triiodothyronine.

The parafollicular cells are primarily located in clusters between follicles but can also be a part of the follicular wall.

Parafollicular cells are larger, oval in shape and have lighter stained cytoplasm than follicular cells. These cells secrete calcitonin.

PARATHYROID GLAND

Sections of parathyroid gland can be seen on slides. In slide parathyroid tissue will be found on one side of the much larger mass of thyroid tissue. To find the parathyroid tissue scan around the periphery of the thyroid tissue at low magnification.

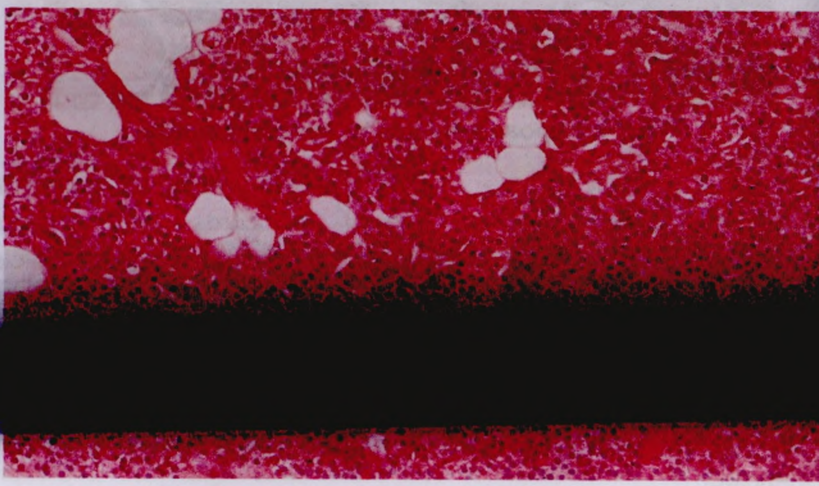

Fig. 15. Parathyroid Gland

The parenchyma of the gland is made up of two identifiable cell types: the predominant chief (or principal) cells (source of parathyroid hormone) and occasional oxyphil cells. Observe the arrangement of chief cells in the parathyroid. The chief cells are arranged as interconnecting cords or clusters, with blood vessels and connective tissue forming the partitions between the cell cords. The capillaries may be more easily seen because erythrocytes have been retained within the lumens. The individual chief cells, seen well, have relatively little cytoplasm, which may be almost unstained or lightly basophilic. The lightly stained cells are thought to be quiescent while the more basophilic cells are believed to be more actively involved in the synthesis and secretion of parathyroid hormone.

In either try to find oxyphil cells. Oxyphil cells are much less numerous than chief cells and can be differentiated from them by the following criteria: larger than chief cells, with more extensive, eosinophilic cytoplasm, nuclei smaller and darker staining, usually occur in isolated groups. Not every specimen in the glass slide sets contain readily identifiable oxyphil cells.

ADRENAL GLAND

The adrenal gland is another "double origin" and double function endocrine organ. The outside layer of the triangle-shaped organ, the **cortex**, is made of the **steroid hormone producing cells**, and secretes cortisol, aldosterone, and adrenal androgens. In the interior is a **medulla** that is part of the autonomic nervous system and is made of the chromaffin cells that secrete [illegible] adrenal gland lies the large central vein.

At low magnification on the adrenal gland, note that the gland is enclosed by a connective tissue capsule and has two principal regions - a cortex and a medulla. The cortex occupies the greatest area on your slide. In many regions of slide you will see only cortex, because some parts of the adrenal lack medulla.

The cortex is made up of three regions or zones: the zona glomerulosa, the zona fasciculata and the zona reticularis. The zona fasciculata is probably the easiest layer to spot as it is a broad zone of cells arranged in straight cords, one or two cells thick, which run at right angles to the surface of the gland. The cells of the fasciculata are lightly stained and have a frothy appearance, due to the extraction of lipid droplets from the cell cytoplasm during tissue processing. Interior to the fasciculata is the zona reticularis, which stains more deeply than the other two regions of the cortex. The cells of the zona reticularis are arranged as anastomosing (reticular or net-like) cords.

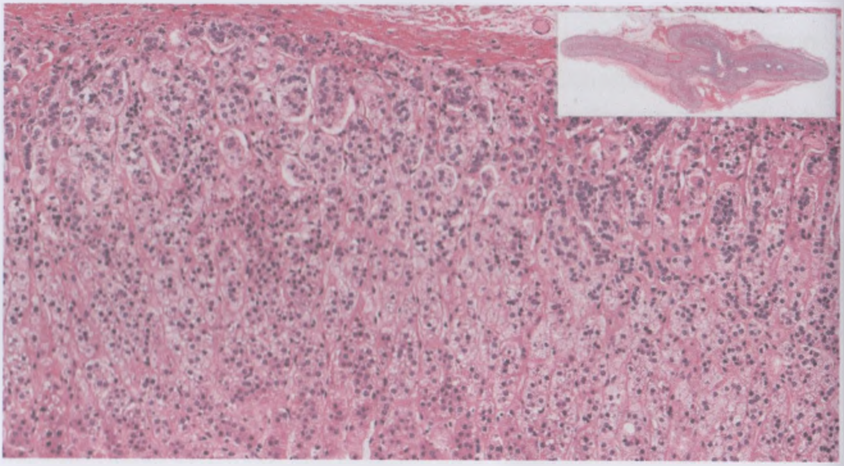

Fig. 16. The cortex adrenal

The zona glomerulosa is found outermost in the cortex and consists of cells arranged in rounded or arched clusters although in the adrenal gland, the zona glomerulosa may not be present around the entire periphery of the cortex. In other species, however, this zone exists as a complete layer around the entire periphery of the cortex, which of the adrenal gland.

Return to the medulla of slide. The medullary cells, source of norepinephrine (noradrenalin) and epinephrine (adrenalin), are often more basophilic than the cells of the cortex. The cells of the medulla are considered to be modified postganglionic sympathetic neurons (derived from neural crest cells). These secretory cells are also called chromaffin cells because their secretory granules (containing norepinephrine or epinephrine) stain brown with potassium dichromate. Note the branches of the central (or medullary) vein in the medulla and review the blood circulation of the adrenal.

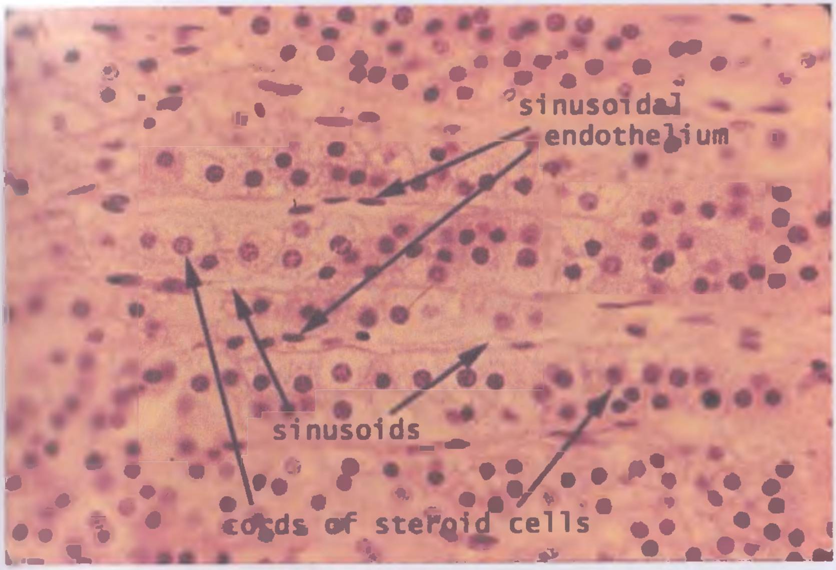

Fig. 17. The zona fasciculata

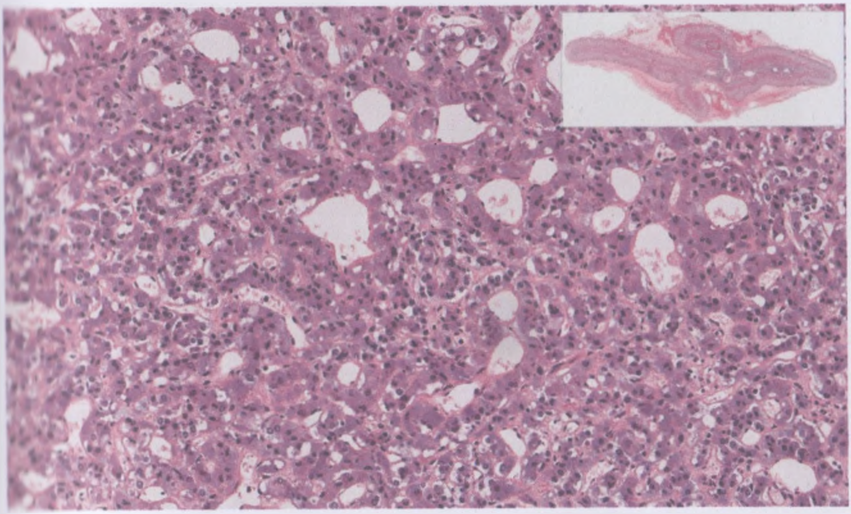

Fig. 18. The medulla adrenal

THYMUS

While production of these immune cells primarily occurs in the bone marrow, education of a special lineage of immune cells takes place in the thymus.

Key facts about the histology of the thymus	
Structure	Divided into thymic lobules separated by connective tissue septae. Each lobule is made up of a peripheral cortex and an inner medulla.
Thymic cortex	Superficial layer: superficial subscapular cells forming a squamous sheath and a blood thymus barrier Middle layer: stellate thymic epithelial and cytoreticular cells Inner layer: squamous cortical thymic epithelial cells which form the corticomedullary barrier
Thymic medulla	A second layer of squamous thymic epithelial cells and cytoreticulum Thymic epithelial cells congregated into Hassall's corpuscles Thymic nurse cells which are responsible for educating thymocytes
Function	Maturation and education of T lymphocytes via positive and negative selection

The thymus is an encapsulated primary lymphoid organ. Histologically, it is divided into subcapsular cortical, cortical, and medullary regions within each lobule, created by the intervening connective tissue septae extending from the capsule.

Gross cross-sectional dissection of the thymus reveals a darker cortical region that is more peripheral to the lighter medullary compartment. The variation in colour intensity is attributed to the density of the thymocytes in each respective area. Therefore, the darker cortex has more T – lymphocytes when compared to the lighter medulla.

Fig. 19. Blood-thymus barrier

There are two major categories of cells within the thymus. These are the thymic epithelial cells and thymocytes. The thymic epithelial cells are endodermal derivatives of the third pharyngeal pouch that further differentiates into specialized epithelium within the cortex and medulla. Overall, these cells are characterized by an eosinophilic cytoplasm containing intermediate filament bundles with pale, ovoid nuclei.

The superficial subcapsular cells are arranged as a continuous squamous sheath that follows the visceral contours of the capsule; even extending within the septae into the lobules and surrounding the vascular beds within it. The cell membranes are tightly held together by desmosomes and occluding junctions. The squamous thymic epithelial cells, along with pericytes and vascular epithelium, form the blood thymus barrier. With this barrier in place, the likelihood of exposing thymocytes to improper antigens is greatly reduced.

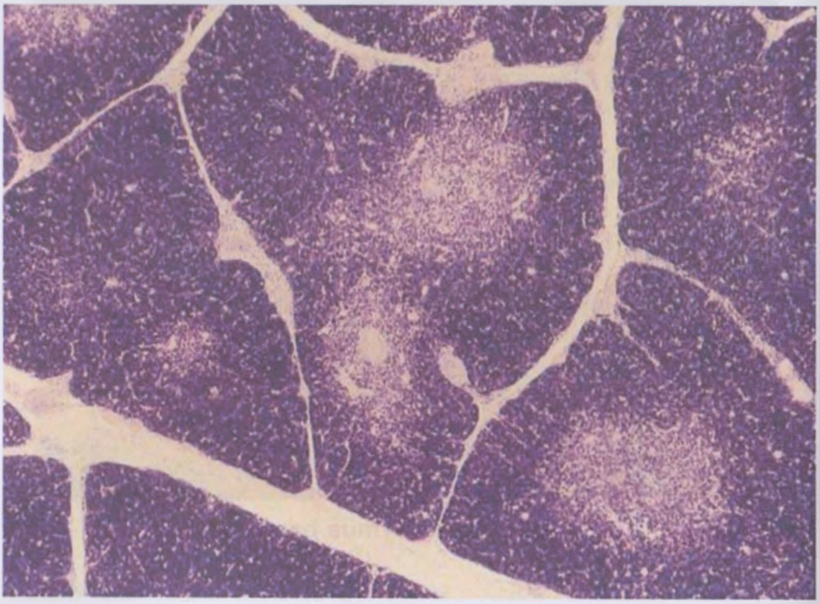

Fig. 20. Thymus

Deep to this layer of cells, within the cortex, are stellate thymic epithelial cells that are filled with keratinized tonofilament anchored together by desmosomes. This architectural arrangement gives rise to the cytoreticulum of the cortex. The cytoreticulum is analogous the collagenous reticular network observed in other lymphoid tissue.

They both facilitate attachment of maturing lymphocytes and surrounding macrophages.

Cytoreticular cells are antigen presenting cells (APC) that express both class I and class II major histocompatibility complex (MHC I and MHC II) proteins that participate in the thymic education program. They also release cytokines that help to create the microenvironment necessary for thymic education.

An inner layer of squamous cortical thymic epithelial cells that are MHC I positive extends into the lobules of the thymus and forms the corticomedullary barrier. This functional partition separates the outer cortex from the inner medulla.

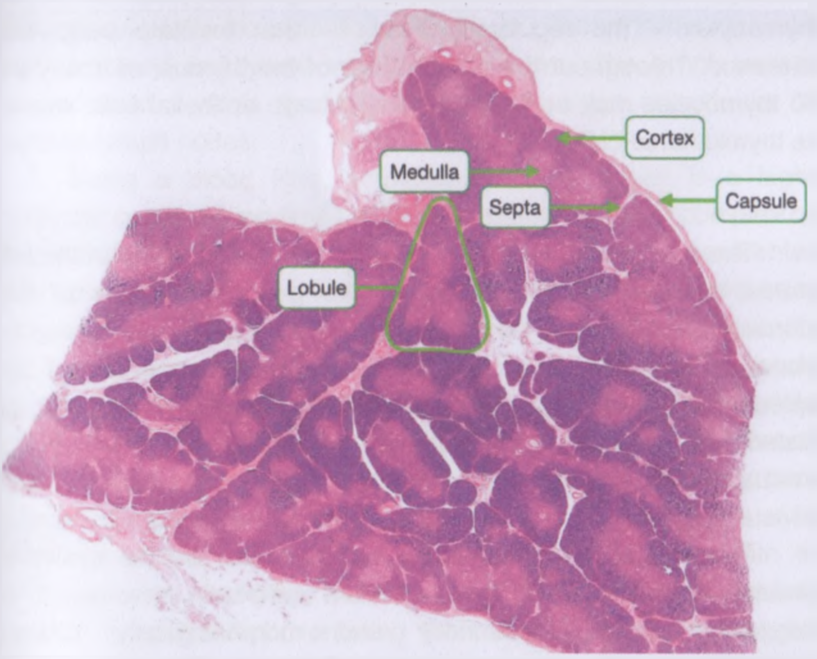

Fig. 21. The thymus is arranged into lobules each with an outer cortex and inner medulla

Within the medulla, there is a second layer of squamous thymic epithelial cells that reinforces the corticomedullary barrier. The medulla also has a cytoreticulum that provides a similar microenvironment for resident dendritic cells, macrophages and more mature thymocytes.

Unique to the thymic medulla is a concentric congregation of thymic epithelial cells known as Hassall corpuscles. They are responsible for the release of cytokines that regulate dendritic activity. Other theories propose that they also remove apoptotic thymocytes. This is supported by the presence of cellular debris at the centre of the whorls that are particularly eosinophilic and partially keratinized. Furthermore, they program a special subset of thymocytes – the regulatory T-cells – that facilitate peripheral tolerance. Throughout the parenchyma of the thymus, as many as 50 thymocytes may be associated with large epithelial cells known as thymic nurse cells.

SPLEEN

The spleen is a dark red to blue-black organ located in the left cranial abdomen. It is adjacent to the greater curvature of the stomach and within the omentum. It is an elongated organ, roughly triangular in cross section. The gross appearance and size of the spleen are variable, depending on the species and the degree of distension; nonetheless, spleen weights can be important in its evaluation. The ratio of splenic weight to body weight remains fairly constant regardless of age and, in rats, is typically around 0.2%.

The functions of the spleen are centered on the systemic circulation. As such, it lacks afferent lymphatic vessels. It is comprised of 2 functionally and morphologically distinct compartments, the red pulp, and the white pulp. The red pulp is a blood filter that removes foreign material and damaged and effete erythrocytes. It is also a storage site for iron, erythrocytes, and platelets. In rodents, it is a site of hematopoiesis, particularly in fetal and neonatal animals. The spleen is also the largest secondary lymphoid organ containing about one-fourth of the body's lymphocytes and initiates immune responses to blood-borne. This function is charged to the white pulp which surrounds the central arterioles. The white pulp is composed of three sub-compartments: the periarteriolar lymphoid sheath (PALS), the follicles, and the marginal zone.

The spleen is surrounded by a capsule composed of dense fibrous tissue, elastic fibers, and smooth muscle. The outermost layer of the splenic capsule is composed of mesothelial cells, which may not be evident on histologic section. Irregularly spaced trabeculae of smooth muscle and fibroelastic tissue emanate from the capsule into the splenic parenchyma. These trabeculae also contain blood and lymph vessels and nerves. The lymph vessels are efferent vessels through which lymphocytes migrate to the splenic lymph nodes.

Being a blood filter, it follows that the spleen is a highly vascular organ. Blood flow through the spleen is rather complex but is an important and sometimes controversial concept. Blood enters the spleen at the hilus via the splenic artery. The splenic artery divides into trabecular arteries located within the trabeculae entering the splenic parenchyma. Small arterioles branch from the trabecular arteries and enter the red pulp where they become central arterioles which are surrounded by lymphoid tissue. Smaller arterioles branch from the central arterioles and feed the white pulp capillary beds. Some of these terminate in the marginal sinus at the junction of the white pulp and the marginal zone, others terminate within the marginal zone, and a few extend beyond the white pulp to terminate in the red pulp. Blood entering the marginal sinus and marginal zone percolates through the marginal zone in the direction of the red pulp. Once through the marginal zone, the blood either flows directly into adjacent venous sinuses whose open ends are continuous with the marginal zone, the so-called «fast pathway», or enters the reticular meshwork of the red pulp, the «slow pathway». As much as 90% of the total splenic blood flow travels through the adjacent venous sinuses, bypassing the reticular meshwork of the red pulp. As the central arterioles continue, the white pulp wanes and they become the penicillar arteries surrounded by red pulp. These give rise to the arterial capillaries, which terminate in the reticular meshwork of the red pulp in rodents. Blood from the red pulp collects in the venous sinuses which enter the trabeculae and merge into the trabecular veins. The trabecular veins then converge at the hilus to form the splenic vein which drains into the hepatic portal system.

The **red pulp** is composed of a three-dimensional meshwork of splenic cords and venous sinuses. The splenic cords are composed of reticular fibers, reticular cells, and associated macrophages. The reticular cells are considered to be myofibroblasts and may play a role in splenic contraction. With electron microscopy, it is apparent that the reticular fibers are actually ensheathed by the reticular cells and their processes. The reticular fibers are composed of collagenous and elastic fibers, microfibrils, reticular cell basal laminae, and unmyelinated adrenergic nerve fibers. Within the spaces between the cords are blood cells, including erythrocytes, granulocytes, and circulating mononuclear cells. Also associated with the splenic cords, are lymphocytes and hematopoietic cells as well as plasma cells and plasmablasts that migrate from the follicles and the outer PALS after antigen specific differentiation. The red pulp macrophages are actively phagocytic and remove old and damaged erythrocytes and blood-borne particulate matter. Extra medullary hematopoiesis is common in rodent red pulp, especially in fetal and neonatal animals. Any combination of erythroid, myeloid, and megakaryocytic cells may be evident.

Venous sinuses can be found throughout the red pulp, including, as mentioned previously, directly adjacent to the marginal zone. They are lined by loose network of endothelial cells which sit on a basement membrane that is sandwiched between the endothelial cells and reticular fibers of the red pulp. The penicillar arteries and arteriolar capillaries are also located in the red pulp, though they are more difficult to identify light microscopically.

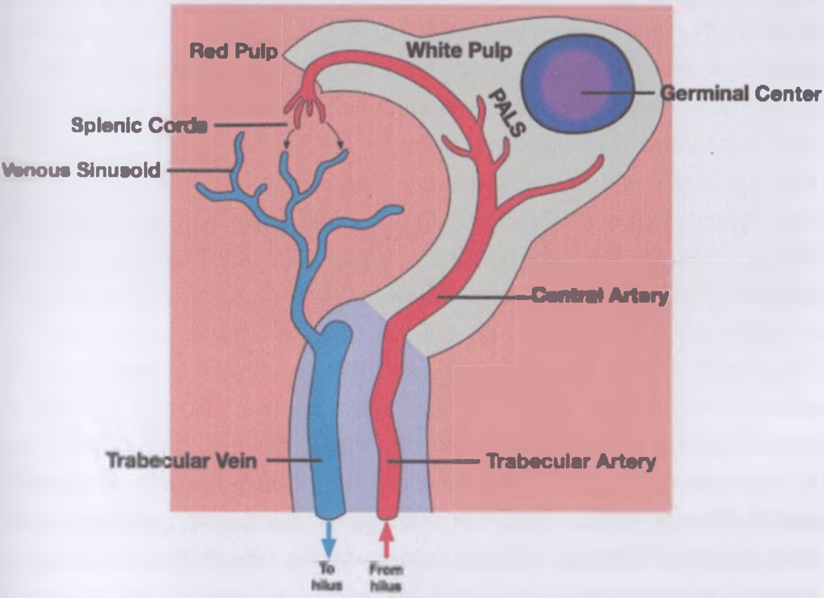

Fig. 21. Blood flows through white pulp and then some is released into red pulp

Various pigments may be present in the spleen. Hemosiderin deposits in the cytoplasm of macrophages in the red pulp, and sometimes in the white pulp as well, are a typical finding. In fact, iron pigments (i.e., hemosiderin and ferritin) are the most common pigments in the macrophages of the red pulp. Iron from the hemoglobin of phagocytized erythrocytes is converted to hemosiderin for storage in the spleen. Ceroid and lipofuscin derived from oxidation of lipids is also typically found in the spleen, though they are less abundant than hemosiderin. Melanocytes containing melanin may be present in the spleen, particularly in black mice, usually in the trabeculae or focally in the red pulp.

The **white pulp** is subdivided into the PALS, the follicles, and the marginal zone. It is composed of lymphocytes, macrophages, dendritic cells, plasma cells, arterioles, and capillaries in a reticular framework similar to that found in the red pulp. As the central arterioles enter the red pulp, they are surrounded by the PALS which are composed of lymphocytes and concentric layers of reticular fibers and flattened reticular cells. The PALS are divided into the inner PALS and the outer PALS. The inner PALS, a T-cell dependent region, may stain slightly more intensely than the outer PALS due to its cellular composition of predominantly small lymphocytes. The difference, however, is not uniformly present and is generally very subtle and difficult to detect by light microscopy. The cells of the inner PALS are largely CD4+ T-cells, though smaller numbers of CD8+ T-cells may also be present, as well as interdigitating dendritic cells, and migrating B-cells. The outer PALS is populated by small and medium lymphocytes (both B- and T-cells), macrophages, and, upon antigenic stimulation, plasma cells. It is an important site of lymphocyte traffic where the formation of plasma cells occurs.

The **marginal zone** is a unique region of the spleen situated at the interface of the red pulp with the PALS and follicles. Considered by many to be a separate compartment rather than part of the white pulp, it is designed to screen the systemic circulation for antigens and pathogens and plays an important role in antigen processing. A band of macrophages, the marginal zone metallophilic macrophages, and the marginal sinus, separate the marginal zone from the PALS and follicles. The marginal zone B-cells are a unique subset of noncirculating B-cells that have an IgM+/IgD− phenotype as opposed to follicular B-cells which are IgM+/IgD+.

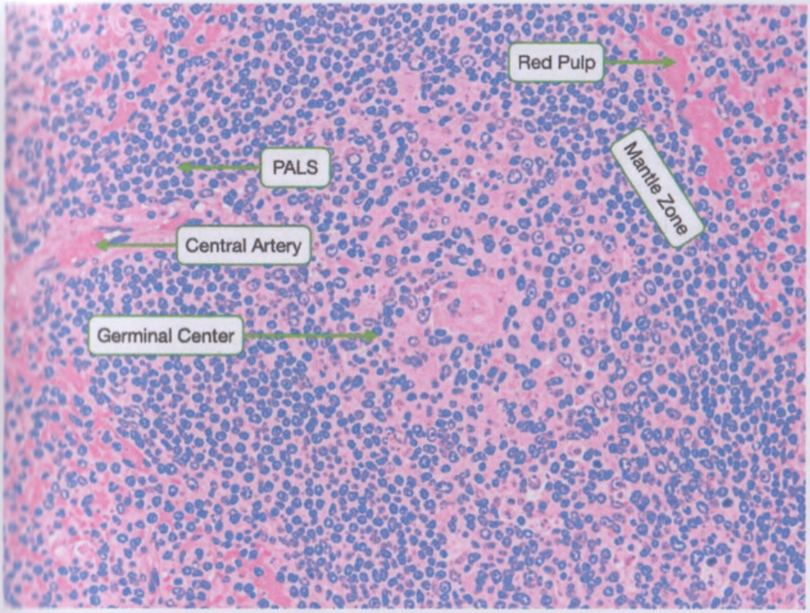

Fig. 22. White pulp contains germinal centers with B-cells surrounded by T-cells and resting B-cells

Species. There are a number of species differences in the gross and histologic appearance of the spleen. In dogs, for example, the spleen is somewhat dumbbell shaped, while in mice and rats, it's more uniform along the longitudinal axis. The spleen in dogs is able to expand to store large numbers of erythrocytes, but it is also capable of rapid contraction. Therefore, its gross appearance is quite variable, ranging from large and dark red to blue-black to smaller and lighter red. The capsule and trabeculae of dogs contains more smooth muscle than that of mice and rats, so the spleens of rodents do not contract as rapidly and tend to vary less in their gross appearance. The splenic artery also differs among species. In dogs, it branches into as many as 25 smaller branches prior to entry into the spleen, while in the rat, there are as many as eight branches.

Vascular arrangements are perhaps the greatest source of species variation in splenic architecture. Species variation in the structure and morphology of the venous sinuses forms the basis for the classification of spleens into two groups, sinusal spleens and nonsinusal spleens. Sinusal spleens are found in rats and dogs and nonsinusal spleens are found in mice. The venous sinuses of sinusal spleens are larger, more abundant, make numerous anastamoses, and have a characteristic wall structure relative to the venous sinuses of nonsinusal spleens. The venous sinuses of nonsinusal spleens are so different, in fact, that some investigators use the term pulp venules rather than venus sinuses. The larger venous sinuses of the rat spleen are far more conspicuous than those of the mouse spleen.

There are also species differences in the arterial vasculature. Schmidt et al. have reported that, in dogs, the arterial capillaries both terminate in the reticular meshwork (open circulation) and empty directly into the venous sinuses with no interruption of the endothelial lining (closed circulation). In dogs, but not rats, the arterial capillaries are surrounded by dense, circumferential clusters of macrophages known as ellipsoids or periarterial macrophage sheaths (PAMS). In dogs, there are very few capillaries within the PALS, as opposed to rats and mice where the PALS have abundant capillaries.

Extra medullary hematopoiesis is more prevalent in spleens of mice than rats. In dogs, hematopoietic tissue is present in the spleen in pathologic conditions such as neoplasia and anemia but may be present in the absence of underlying disease. When the hematopoietic tissue is predominantly myeloid, the term myeloid hyperplasia may be applied. The incidence of splenic myeloid hyperplasia in the absence of underlying disease was 4% in beagle dogs in one study.

Though there is a lot of individual variation, mice tend to have a greater proportion of white pulp than rats, but the follicles and marginal zone of mice are less distinct than those of rats. In rats, the marginal zone comprises up to 28% of the splenic volume and is the largest B-cell region in the spleen. Approximately one-third of the B-cells in the rat spleen have the marginal zone B-cell phenotype, whereas in the mouse, only 15% of the splenic B-cells have this phenotype. Though the region where the marginal sinus is located is more consistently discernible in rats, electron microscopic studies show that the marginal sinus is up to 6 times larger in mice.

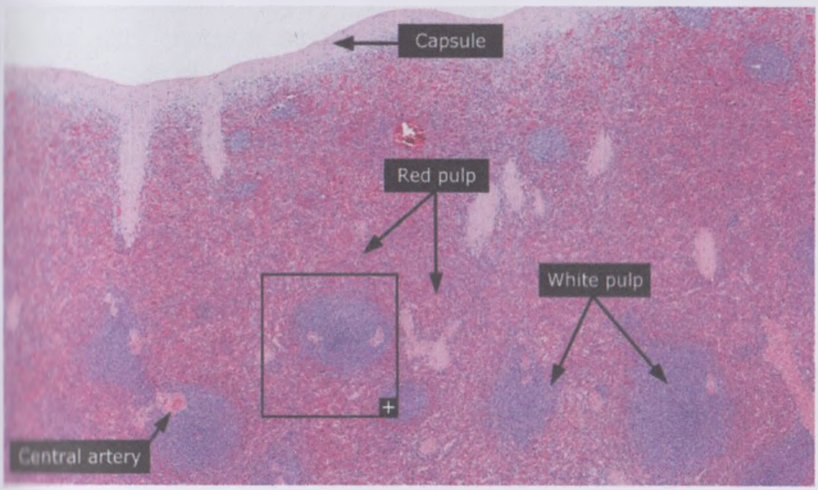

Fig. 23. Spleen

LYMPH NODE

Lymph nodes facilitate the interaction between antigens, antigen presenting cells, and lymphocytes to generate humoral immune response. Lymph nodes occur along the course of the lymphatic vessels that drain lymph from organs and tissues. They filter the lymph before it drains back to the bloodstream and are therefore, in an ideal position to collect antigens from local infections. Normally, they are only a few millimeters in diameter. However, when an immune response is initiated against antigens, the lymphocytes within the lymph nodes undergo activation and proliferation, causing the nodes to enlarge.

Cross-section of Lymph Node. Lymph nodes are usually bean-shaped, with an indented region known as the hilum. They are covered by a collagenous capsule that extends into the body of the node as trabeculae. The body of the lymph node is divided into an outer cortex and an inner medulla. The cortex contains a high concentration of lymphocytes while the inner medulla is less cellular. The lymphocytes in the cortex self-organized into secondary follicles in response to foreign antigen. Follicles are where B-cells mature and proliferate. A paracortex is also defined in lymph nodes as a site where T-cells accumulate.

Lymph from the extracellular space carries antigens and antigen presenting cells, such as dendritic cells, from the tissues to the lymph nodes. The lymph enters the node at several points along the lymphatic system through afferent lymphatic vessels. These vessels pierce through the capsule and drain into the space below, known as the sub-capsular sinus. From the sub-capsular sinus, the lymph drains toward the medulla via channels called cortical sinuses. The sinuses are lined by endothelial cells. After reaching the medulla, the lymph drains into a complex network of medullary sinuses. The medullary sinuses converge at the hilum and drain into the efferent lymphatic vessels.

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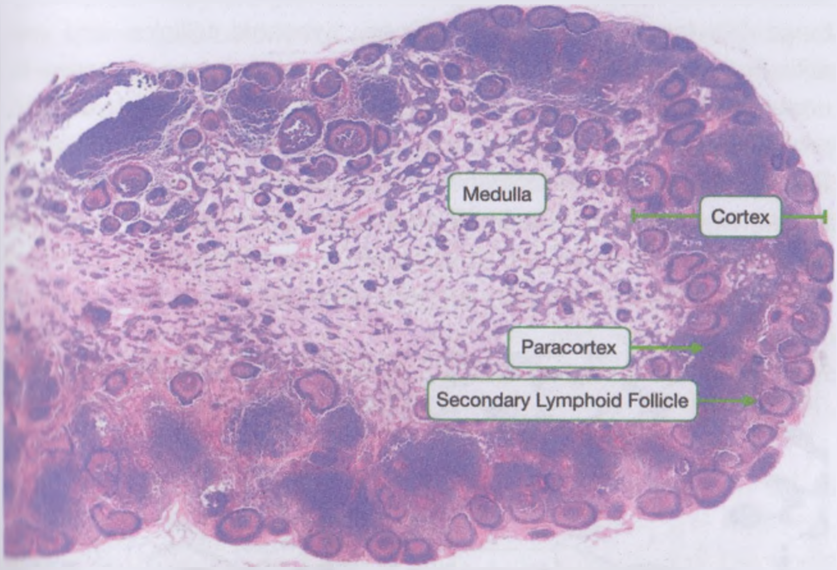


Fig. 24. The lymph node is structurally and functionally divided into a cortex, paracortex and medulla

Macrophages in the parenchyma of the lymph nodes sit underneath the sinuses and extend cellular processes into the sinus channels. These processes capture antigen which is then brought into the parenchyma of the lymph node where it can be sampled by lymphocytes.

This is a high-power view of the lymph node capsule and sub capsular sinus. Note the afferent lymphatic vessels traversing the capsule. The lymphatic vessels contain valves, which are clearly seen in this slide. The sub capsular sinus is lined by a layer of endothelial cells. Beneath the endothelial cells are macrophages that retrieve antigen from the lymph in the sub capsular sinus.

These macrophages cannot be distinguished in histological images. In the cortex, B-lymphocytes are localized in lymphoid follicles just beneath the capsule. In absence of an active immune response, these follicles are known as primary lymphoid follicles and are difficult to distinguish histologically. When an immune response is underway, the follicles develop germinal centers that contain proliferating and maturing B-cells that are responding to antigen. Surrounding the germinal centers is the mantle zone that contains resting and memory B-cells. T-cells also reside close to germinal centers and help select and stimulate B-cells. Follicles with germinal centers are called secondary lymphoid follicles.

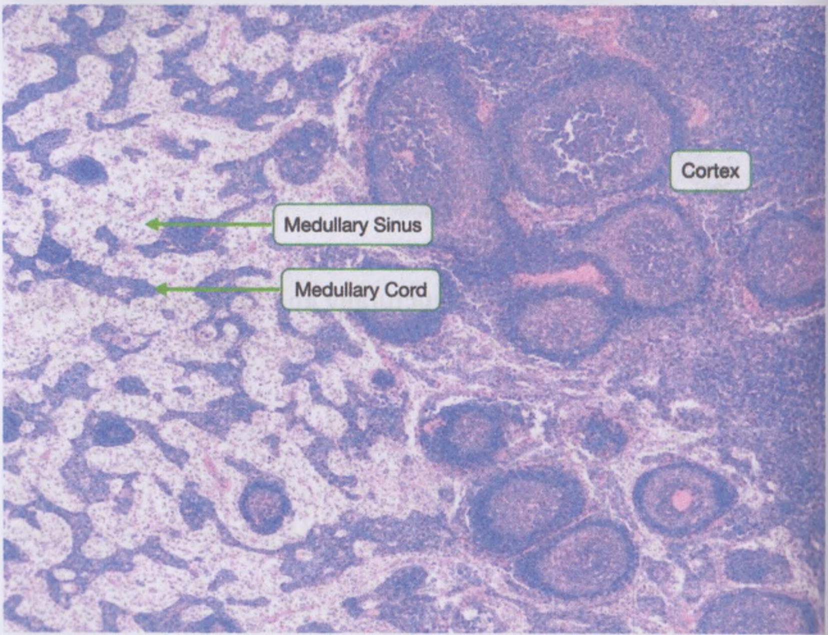


Fig. 25. The medulla contain macrophages and B-cells arranged in cords and sinuses that contain lymph

Secondary follicles with germinal centers are not unique to lymph nodes but can form anywhere an immune response is generated. They are prominent along the wall of the intestine and in the spleen (see below) but can also form in other organs during an immune response to an infection. When occurring outside the lymph node these follicles are usually called secondary lymphoid organs.

The paracortex lies between the cortex and medulla and contains a high concentration of T-cells. Another feature of this region is the high endothelial venule, where circulating lymphocytes leave the bloodstream to enter the lymph node. High endothelial venues can be distinguished by their cuboidal endothelial cells. Adhesion molecules such as selectins and integrins mediate attachment of lymphocytes to endothelial cells. In a T cell-dominant immunological response, one may observe expansion of the paracortical region.

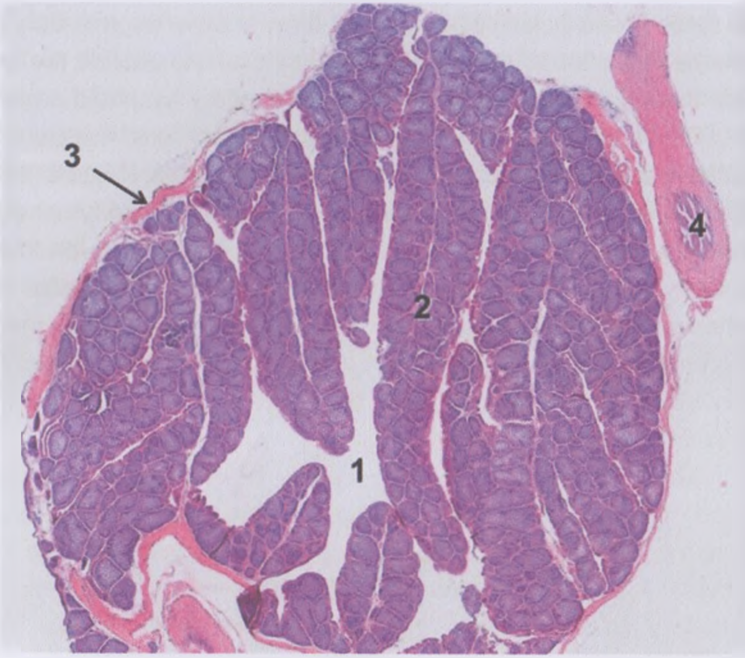
The medulla contains aggregates of lymphoid tissue called medullary cords. The cords contain macrophages and antibody-secreting B-cells called plasma cells. Lymph flows past the cords through lymphatic channels called medullary sinuses. The medullary sinuses merge into efferent lymphatic vessels, which carry the lymph away from the node.

BURSA OF FABRICIUS

The bursa of Fabricius (bursa cloacalis) is present in birds only. It is a blind sac-like dorsal diverticulum of the wall of the proctodeum of the cloaca in which maturation of B lymphocytes takes place.

The bursa regresses with the onset of age or when reproductive activity (laying of eggs in females) starts.

The overall shape varies according to species at the bursa of chickens and pigeons is oval shaped, ducks have a more elongated bursa. In most birds, the bursa is connected to the proctodeum with a small stalk. In ratites *(Struthioniformes)*, the bursa is an integral part of the mucosa of the proctodeum.



1 – lumen; 2 – bursal fold (plica bursalis); 3 – bursal capsule (capsula bursalis); 4 – oviduct

Fig. 26. Bursa of Fabricius

TESTES

Testes are the place of sperm production. Each testis is divided into lobules, each containing one to four seminiferous tubules. The **seminiferous tubules** are tightly coiled, which adds to their length, and have a hollow center. Inside the seminiferous tubules are germ cells, called **spermatocytes,** in different stages of development and supporting cells called **sustentacular cells** or **Sertoli cells**. Germ cells are in close contact with Sertoli cells, an arrangement similar to marbles (germ cells) pushed into playdough

(Sertoli cell). Sertoli cells secrete molecules that promote sperm production and control germ cell survival.

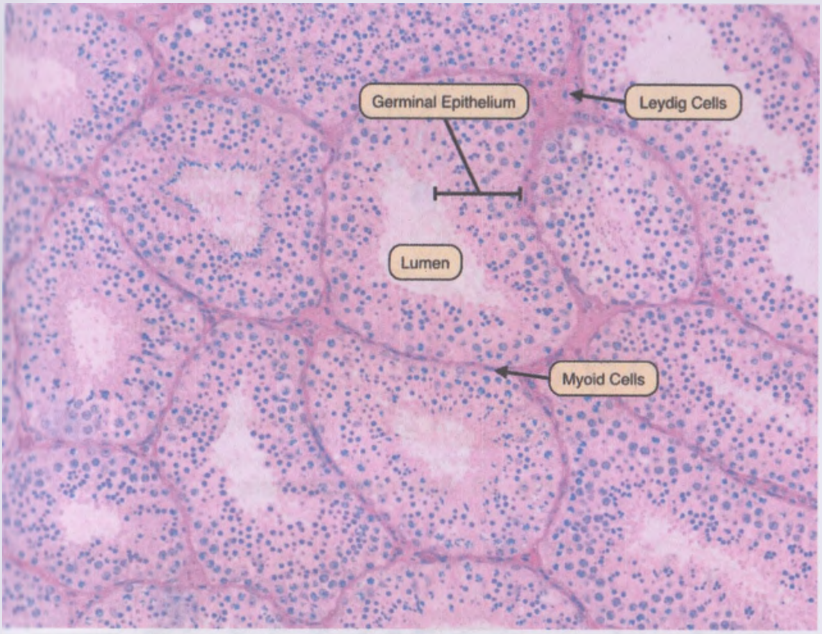


Fig. 27. Testes

The youngest spermatocytes, **spermatogonia**, are closest to the perimeter of the tubule, and the most mature spermatocytes, **spermatozoa,** or sperm with tails, are closest to the middle.

Spermatogonia are the largest of the germ cells, with rounded granular nuclei. During maturation, spermatocytes lose organelles and cytoplasm, and become smaller in size. The mature sperm – with the commonly known shape of a head with DNA, mitochondria along the neck and a long tail – lie closest to the lumen, have elliptical nuclei and no visible cytoplasm. Sometimes the tails are visible but not easy to find. Sperm and their tails are best observed in fresh preparations of ejaculate known as a **sperm count**. Seminiferous tubules merge to form **rete testis**, a network of straight tubules that progress to the epididymis, and then to subsequent ducts, ending with the urethra.

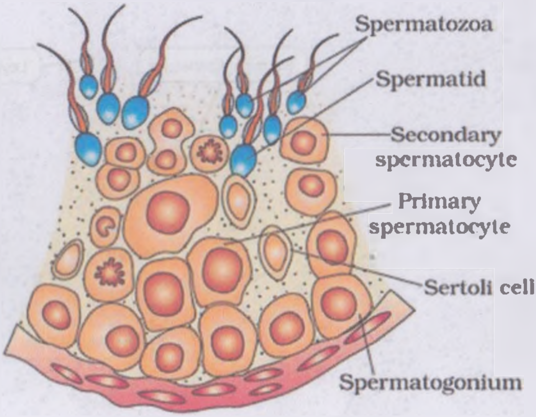


Fig. 28. Spermatogenesis

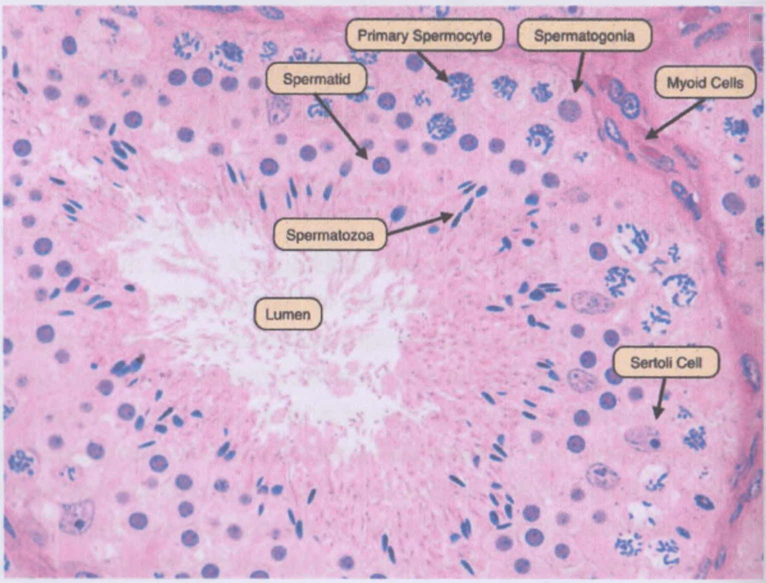


Fig. 29. The germinal epithelium

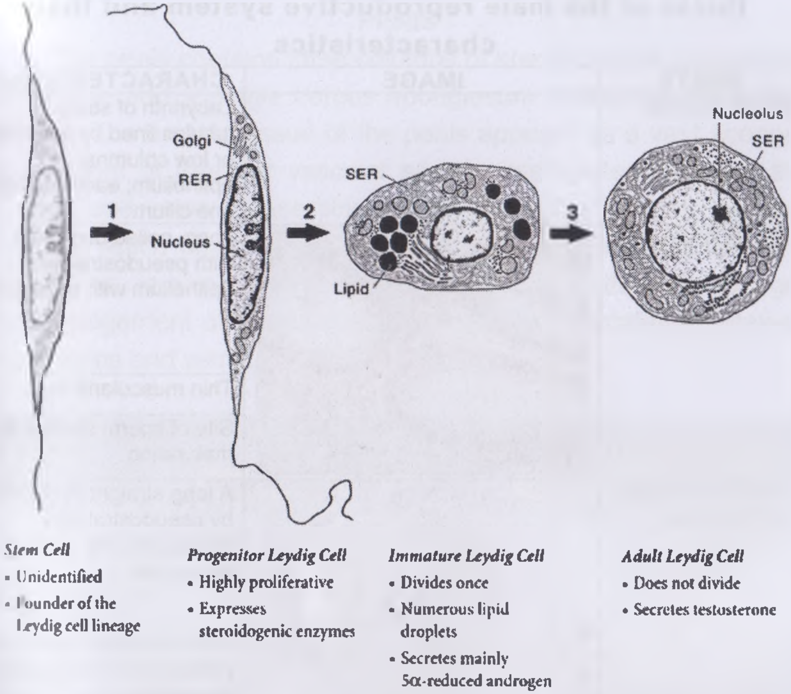
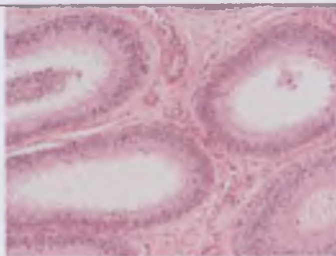
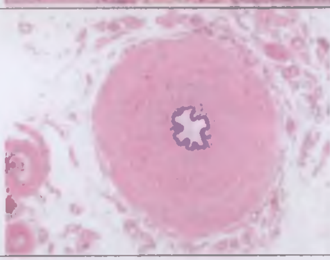


Fig. 30. Leydig cell development and function

Leydig Cells. Interstitial or Leydig cells are located in the connective tissue surrounding the seminiferous tubules. They produce testosterone, the male sex hormone responsible for the growth and maintenance of the cells of the germinal epithelium and the development of secondary sex characteristics. Leydig cells often display cytoplasmic crystals of Reinke, the function of these crystals is unknown.

Ducts of the male reproductive system and their characteristics

DUCTS	IMAGE	CHARACTERISTICS
RETE TESTIS		Labyrinth of straight tubules lined by cuboidal or low columnar epithelium; each cell has one cilium
EPIDIDYMIS		Long, coiled duct lined with pseudostratified epithelium with stereocilia
		Thin muscularis layer
		Site of sperm storage and maturation
DUCTUS (VAS) DEFERENS		A long straight duct lined by pseudostratified epithelium with some stereocilia
		Thick muscular layer with peristalsis to move sperm toward ampulla
AMPULLA OF DUCTUS DEFERENS		A dilated portion of ductus deferens; same characteristics as ductus deferens
EJACULATORY DUCT		Narrower part of the ductus deferens that runs through the prostate gland; same characteristics as ductus deferens
URETHRA		A passage lined by stratified columnar or stratified cuboidal epithelium; moderate thickness muscularis

PENIS

The penis contains three columns of erectile tissue: two corpus cavernosa and a single corpus spongiosum containing the penile urethra. The erectile tissue of the penis appears as a vast sponge-like system of irregular vascular spaces intercalated between the arteries and veins. These sinuses receive blood from the helicine arteries, which dilate during erection to engorge the sinuses with blood. This, in turn, restricts venous outflow. Note the vast sponge-like arrangement of irregular vascular spaces intercalated between the arteries and veins.

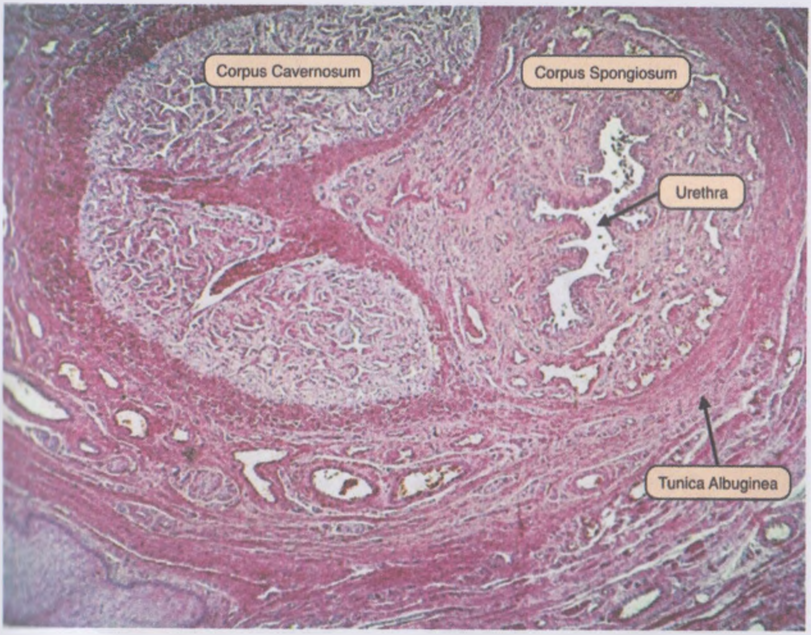


Fig. 31. Penis

The secondary oocyte, having undergone the first meiotic division, is located eccentrically. It is surrounded by the zona pellucida, and a layer of several cells known as the corona radiata. When released from the Graafian follicle and into the oviduct, the ovum will contain three layers: oocyte, zona pellucida and corona radiata.

The corpus luteum is the endocrine remains of the collapsed follicle. The center contains the remains of the blood clot that formed after ovulation. Surrounding the clot are glanulosa lutein cells and on the outside theca lutein cells. The granulosa lutein cells have an appearance characteristic of steroid-producing cells, with pale cytoplasm indicating the presence of lipid droplets. Theca lutein cells are smaller and more deeply stained. If fertilization and implantation ensue, the corpus luteum will be maintained by hCG and remain active as the corpus luteum of pregnancy. If fertilization does not occur, the corpus luteum involutes to form the corpus albicans that is filled with fibrous tissue. The secretory cells of the corpus luteum degenerate and are phagocytoses by macrophages.

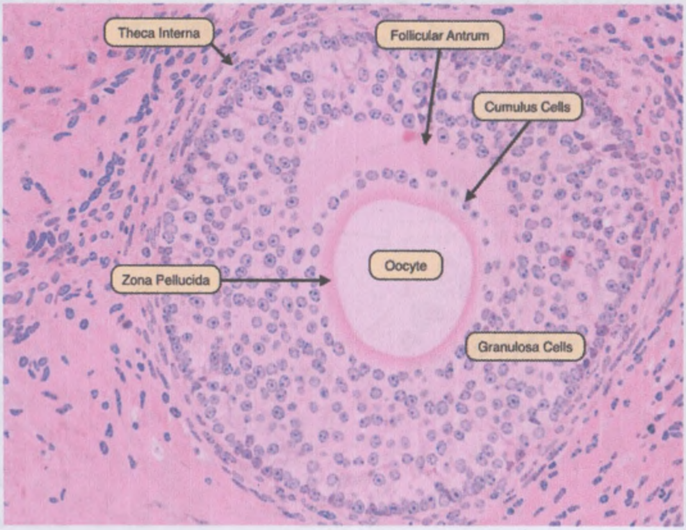


Fig. 34. Secondary Follicle

Degeneration of follicle (atresia) can occur at any stage of development. The granulosa cells undergo apoptosis and consequently, the oocyte degenerates. The basement that separated the oocyte from granulosa cells often thickens to become the glassy membrane. Fibrous material replaces the granulosa cells.

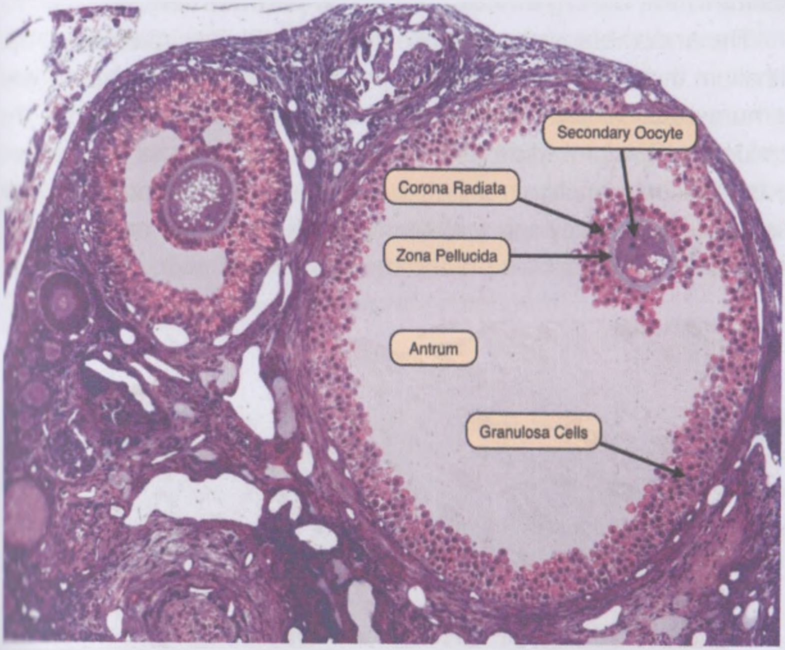


Fig. 35. Graafian Follicle

Degeneration of follicle (atresia) can occur at any stage of development. The granulosa cells undergo apoptosis and consequently, the oocyte degenerates. The basement that separated the oocyte from granulosa cells often thickens to become the glassy membrane. Fibrous material replaces the granulosa cells.

UTERUS

The uterus is the muscular organ required for the maintenance of pregnancy. The upper part of the uterus is the body. The cervix is the narrow lower portion that projects to the vagina. The wall of the uterus has three layers. Going from the inside, they are the **endometrium, the myometrium** and **the perimetrium**.

The endometrium, or mucosa, is covered with simple columnar epithelium that rests on the lamina propria. Under the mucosa there are numerous tubular uterine glands that extend deep into the submucosa. Endometrium undergoes the cyclical changes called the uterine or menstrual cycle, that prepare the endometrium for pregnancy. If the pregnancy does not occur, the endometrium gets removed during menstruation and the cycle starts over.

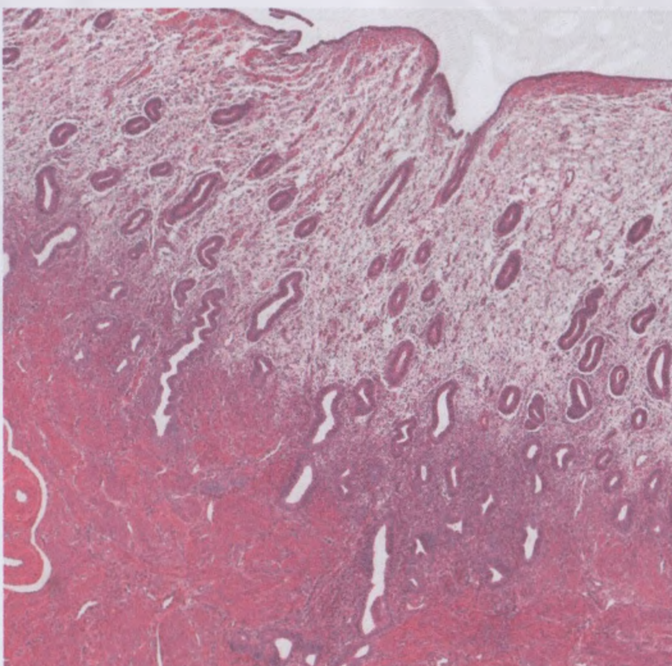


Fig. 36. Endometrium

The **proliferative stage** follows menstruation and is the stage of endometrium growth and repair. The uterine glands are tubular, relatively straight and narrow. Glands are distant from one another.

The **secretory stage** follows the proliferative stage and is the preparation for implantation of the embryo. The endometrium is thicker, glands are closer to one another and are frequently distended with secretions. They have a characteristic convoluted and "saw-toothed" appearance.

The **myometrium** is a thick layer of smooth muscle arranged in two layers, an inner circular layer and an outer longitudinal layer. Myometrium is responsible for the uterine contractions during labor.

The **perimetrium** is the outermost layer and is composed of loose connective tissue, lymphatics and small arteries and veins with overlying mesothelium cells of peritoneum.

SKIN

Skin covers the outer surface of the body and is the largest organ. Skin and it's accessory structures (hair, sweat glands, sebaceous glands, and nails) make up the **integumentary system**. Its primary functions are to protect the body from the environment and prevent water loss.

Skin is classified into two types:

- **Thick skin** - covers the palms of the hands and the soles of the feet.
- **Thin skin** - covers the rest of the body.

Skin consists of two layers:

- **Epidermis** - outer layer of stratified squamous keratinized epithelium.
- **Dermis** - underlying layer of dense, irregular connective tissue that contains other structures (such as hair follicles and sweat glands).

Deep to the dermis is the **hypodermis**, a layer of varying thickness of loose connective tissue and adipose tissue.

Thick skin is only found on the palms of the hands, and the soles of the feet, locations subjected to considerable abrasion. It has a thick epidermis and contains sweat glands but lacks hair follicles and sebaceous glands.

SKIN LAYER	SKIN FEATURES
STRATUM CORNEUM	A layer of dead corneocytes. No nuclei or organelles are present, just dried membranes and keratin fibers. Is thicker in thick skin than in thin skin.
STRATUM LUCIDUM	A thin, transparent layer of lightly stained, flattened keratinocytes. Keratinocytes in this layer have lost their organelles. Keratohyalin has been transformed into translucent eleidin. **Remember, stratum lucidum is not present in thin skin.**
STRATUM GRANULOSUM	A thin layer containing keratinocytes that are filled with darkly staining keratohyalin granules. Keratinocytes are semi-dry and flat, with elongated nuclei.
STRATUM SPINOSUM	Thickest of the epidermal layers. A few rows of irregular, polygonal-shaped keratinocytes that change from almost cuboidal to flat, as they move away from the stratum basale. The nuclei are round, and cells have visible rings of pink-stained cytoplasm.
STRATUM BASALE	The first layer of cells on the basal membrane. A single layer of cuboidal cells, interspersed with melanocytes that contain brown-colored granules of melanin.

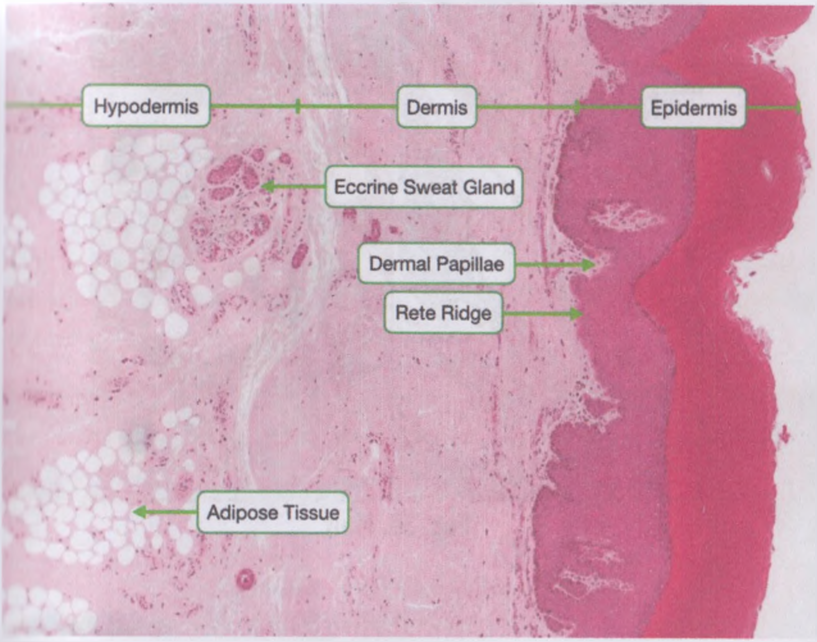


Fig. 37. Skin

HAIR

Hair is present over most of the body and plays an important role in regulating body temperature and absorbs UV light. Hair is composed of concentric layers of epithelial cells that undergo different degrees of keratinaztion. The hair follicle is where hair production and growth of occur. The hair bulb contains stems cells that will differentiate into the different layers of epithelial cells that make up hair. Although the structures of hair are derived from epithelial cells in the epidermis, cells in the dermis play a critical role in regulating the proliferation and differentiation of epithelial cells in the hair bulb. Melanocytes transfer melanosomes to cells in hair which gives hair its color.

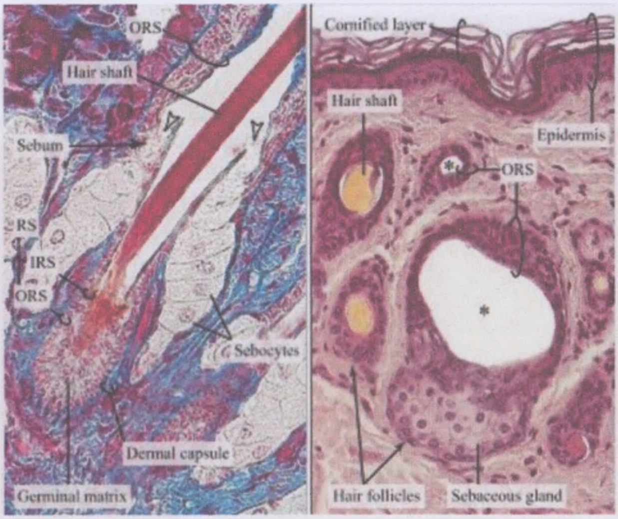


Fig. 38. Hair

SEBACEOUS SWEAT GLAND

Sebaceous glands are pear-shaped glands that secrete an oily substance called sebum, which moisturizes and waterproofs hair. They are usually attached to hair follicles near the arrector pili muscle, which causes hair to "stand up". The glands connect with the hair follicle via a short duct called the pilosebaceous canal.

Fig. 39. Sebaceous glands

SENSORY STRUCTURES OF SKIN

Skin contains a several different types of sensory structures which allows it to detect a variety of mechanical forces and changes in the external environment.

The epidermis contains two major types of sensory structure. The first is free nerve endings which are the termini of sensory neurons that extend axons from the spinal cord. Free nerve endings detect temperature, light pressure and tissue damage.

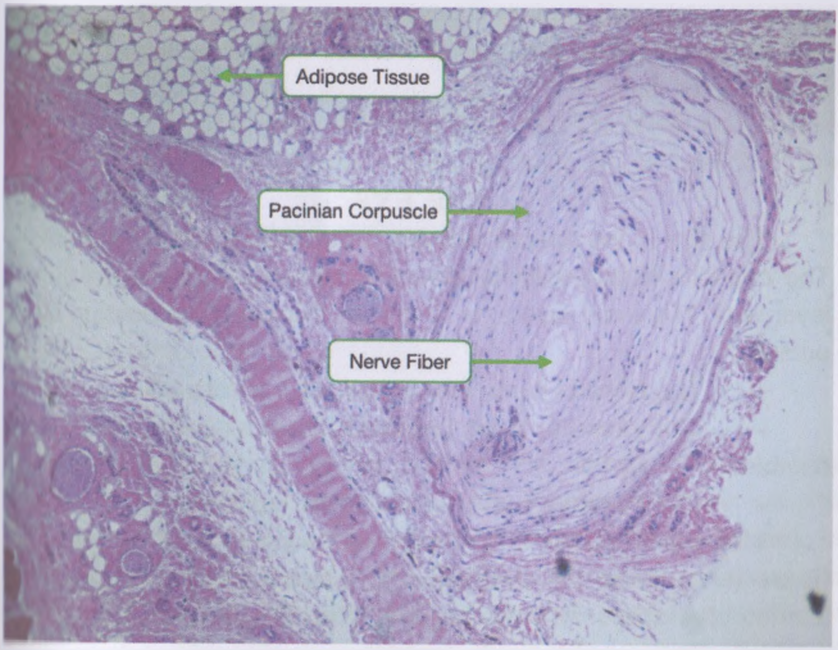


Fig. 40. Pacinian corpuscles

The second sensory structure are Merkel cells that reside in the stratum basale. These cells respond to low-frequency vibration and very small displacements. When stimulated, Merkel cells release serotonin from intracellular granules onto adjacent nerve terminals. These afferent nerves then transmit this signal back to the spinal cord. Merkel cells have a clear cytoplasm with small granules and are difficult to distinguish from melanocytes.

Sensory structures are also found in deeper layers of skin. Meissner's corpuscles are found in the dermis at the very tips of dermal ridges. The corpuscles detect light touch and are composed of a collagenous capsule that surrounds several support cells and sensory nerve fibers.

Pacinian corpuscles are large encapsulated nerve structures that reside in hypodermis. These corpuscles are sensitive to deep pressure and course touch. The corpuscles contain several layers of support cells, thin collagen fibers and interstitial fluid around a central nerve fiber.

THE EYE

The eye is the special sensory organ that gives rise to vision. The eye is a hollow, slightly elongated sphere formed by a three-layer wall. The three layers, or tunics, of the eye are, counting from outside:

- The **fibrous tunic** that comprises the sclera and cornea.
- The **vascular tunic** that forms the iris, ciliary body, and choroid.
- The **nervous tunic**, which is also known as the retina.

Inside the eyeball, the lens is suspended in place by **zonular fibers** (also called the **suspensory ligament**), which divides the interior of the eye into two regions, the **anterior** and **posterior cavities**. The anterior cavity is further divided into anterior and posterior chambers by the iris, creating three separate but communicating, fluid-filled spaces within the eye.

- The **anterior chamber** that extends from the posterior surface of the cornea to the iris.

- The **posterior chamber** that extends from the iris to the front surface of the lens.
- The **vitreous chamber** that extends from the posterior surface of the lens to the retina.

The anterior and posterior chambers are filled with the **aqueous humor**, a watery fluid similar to plasma, while the vitreous chamber is filled with the **vitreous body**, a translucent, gel-like substance that is also called **vitreous humor**.

The fibrous tunic is comprised of two parts: the translucent **cornea**, in the front of the eyeball, and the opaque, white **sclera**, in the back. Cornea and sclera differ primarily in the arrangement of their collagen fibers, which causes the difference in their transparency.

The cornea focuses incoming light onto the retina and serves to protect the eye. The microscopic layers of the cornea, from the outside in, are:

- stratified squamous epithelium.
- Bowman's membrane (also called the anterior limiting membrane).
- stroma.
- Descemet's membrane.
- simple squamous epithelium.

On its external, convex surface, the cornea is covered by stratified squamous epithelium. The innermost layer of the epithelium is columnar and lies on the **Bowman's membrane**. In histological slides stained with H/E, the Bowman's membrane is a solid pink layer directly under the epithelium. The **stroma**, or core of the cornea, is a connective tissue made from parallel layers of collagen fibers that are produced by resident fibroblasts. In histological slides, the clearly visible collagen bundles of the stroma are stained pink. The darker spots in the stroma are the nuclei of the fibroblasts. The internal, concave surface of the cornea is covered by simple squamous epithelium resting on **Descemet's membrane**.

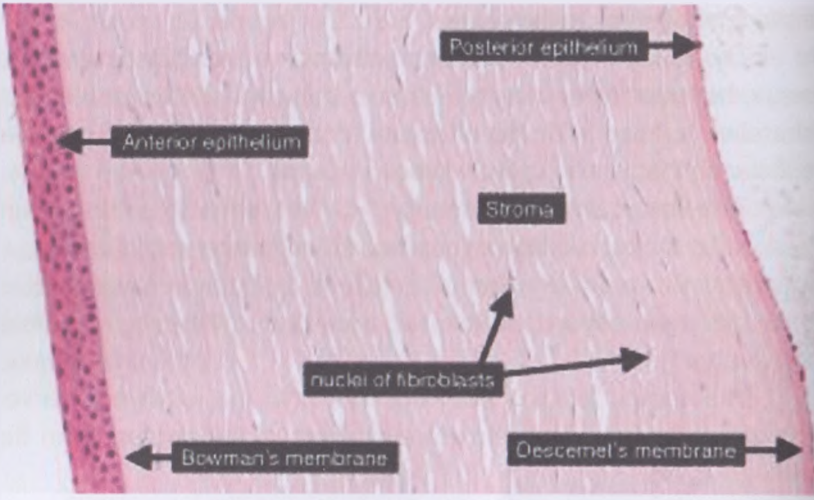


Fig. 41. Cross section of cornea

The cornea has no blood vessels, but does contain nerve fibers, including those that sense pain. The cornea and the visible parts of sclera are loosely covered by the **conjunctiva**, a membrane that extends to the internal surface of the **palpebrae**, or eyelids. The conjunctiva lubricates the eye and protects it from drying. On the slide below, the conjunctiva is visible as the folded membrane on the left and is formed from connective tissue, with stratified squamous epithelium on its surface. The space between the conjunctiva and cornea is filled with tears, which are produced by the **lacrimal apparatus**.

The sclera is the white part of the fibrous tunic and covers the majority of the eyeball. The place where the cornea and the sclera join is called the **limbus**. The sclera is made of connective tissue composed of bundles of collagen and elastic fibers. These fibers are less organized than in the cornea, and that contributes to opacity. The main cells in the scleral stroma are fibroblasts.

In contrast to the cornea, the sclera has blood vessels; it also has sensory nerve fibers. The visible part of the sclera, in the front of the eye, is covered by the conjunctiva. In the back, the sclera is penetrated by the optic nerve exiting the eyeball.

The vascular tunic, also known as the **uvea**, is the layer of the eye situated between the outer fibrous tunic and the inner nervous tunic. The vascular tunic is comprised of three parts:

- the iris;
- the ciliary body;
- the choroid.

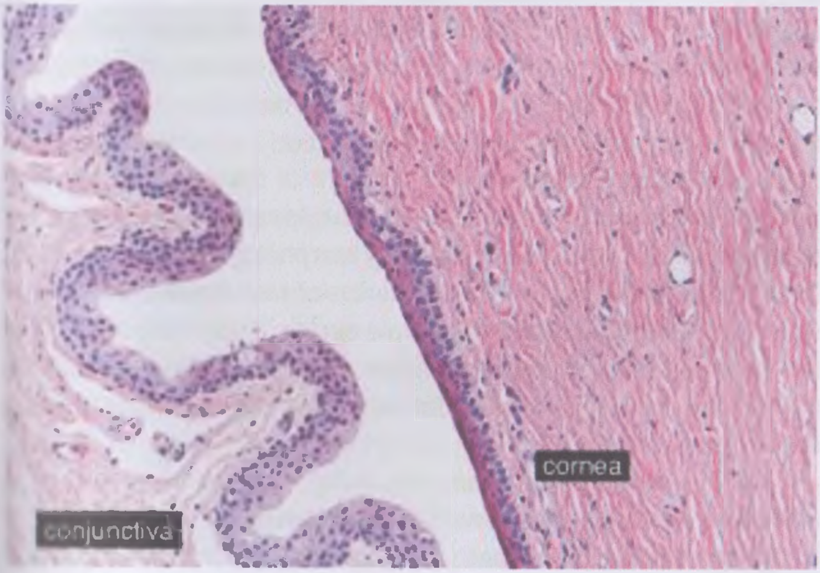


Fig. 42. Conjuctiva and cornea

The **iris** is the anterior portion of the vascular tunic and is visible through the cornea. The iris divides the anterior cavity of the eye into the anterior and posterior chambers. The iris has a muscle located in its stroma that, by constricting and relaxing, changes the size of the pupil, limiting or increasing the amount of light that enters the eye and projects onto the retina.

The color of the iris depends on the presence of melanocytes in the stroma and in the epithelium that covers the iris. In brown eyes, pigment is present both in the stroma and the epithelium; in blue eyes, pigment is only present in the epithelium. In albino eyes, melanin is absent in both the stroma and the epithelium. The irises appear red, however, because the blood vessels of the inner eye can be seen through these translucent irises.

The **ciliary body** is the part of the vascular tunic that is adjacent lens. It consists of a ring of **ciliary processes** – finger-like projections of vascular tissue covered by the **ciliary epithelium** that secretes the aqueous humor which fills the anterior and posterior chambers of the eye. The ciliary body also includes a layer of muscle underneath the ciliary processes that controls the shape of the lens. This is different than the muscle that controls the size of the pupil. On the slide above, the ciliary body is circled; the image below provides a magnified view.

In histological slides, the retina appears as a ten-layered structure whose layers are defined by morphological characteristics. These include the presence or absence of pink-stained fibers or of cell nuclei, which are visible as purple circles. Some cells might form two or even three neighboring layers. Based on how it appears in the microscope, retina has the following layers, proceeding from the chorion to the vitreous body:

- retinal pigment epithelium;
- layer of photoreceptor cells (rods and cones);
- outer limiting membrane;
- outer nuclear layer;
- outer plexiform layer;
- inner nuclear layer;
- inner plexiform layer;
- ganglion cell layer;

- nerve fiber layer;
- inner limiting membrane.

Adjacent to the choroid, the outermost layer of the retina is the **retinal pigment epithelium**, a cuboidal epithelium that contains melanin and provides nourishment to the retina. Projections of these cells, especially rich in melanin granules, extend between the outer segments of rods.

KIDNEY

The structural unit of urine production in the kidney is a **nephron**. The nephron is a microscopic structure that is made of blood capillaries and a set of tubules made of kidney epithelium. Capillaries bring blood to the nephron where is gets filtered through the **filtration membrane** into the **capsular space**. From the capsular space “future urine”, called **primary filtrate**, will pass through the system of microscopic tubules where the composition of urine will be adjusted to the current needs of the organism. Once urine passes to the **renal pelvis** urine cannot be adjusted anymore. It can only be transported and removed.

On the longitudinal section, the kidney has two characteristic layers: the cortex and the medulla. The **cortex** is located on the outside and is fairly uniform, while the **medulla** is organized into **renal pyramids** spaced by **renal columns**. The bottom of the pyramid is turned toward the cortex. At the tip of each pyramid are holes where the papillary ducts open to the renal pelvis.

The renal cortex contains most of the glomeruli and numerous cross sections of the tubules. The nephron tubules are made of simple cuboidal epithelium. A distinct, often visible on the histological sections, basement membrane surrounds each tubule.

The medulla only has tubules-mostly loops of Henle and collecting ducts-and does not contain glomeruli.

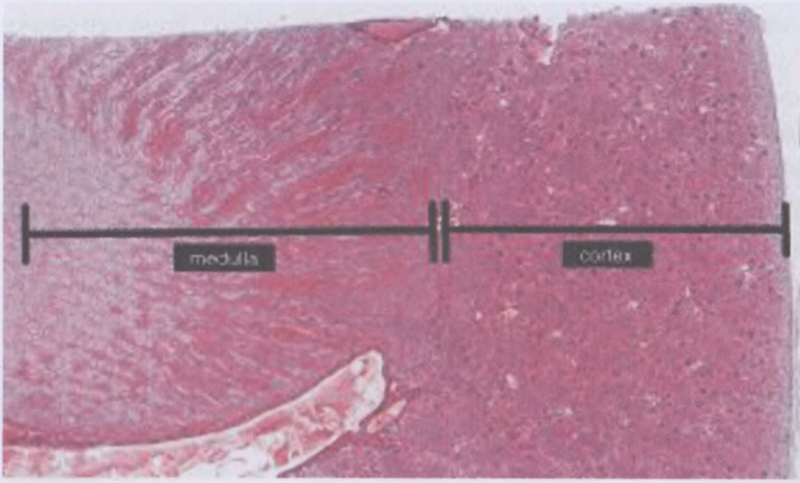


Fig. 43. Kidney

The structural and functional unit of urine production in the kidney is a **nephron**. The nephron is a microscopic structure that is made of blood capillaries and a set of tubules made of kidney epithelium. Capillaries bring blood to the nephron where it gets filtered through the **filtration membrane** at the **renal corpuscle**.
The renal corpuscle has two parts, the **glomerulus** of capillaries in the middle, and a **glomerular (Bowman's) capsule** that wraps up around the glomerulus like a chalice. Between the glomerulus and the capsule is the **capsular space** where the **primary filtrate** (future urine) gathers before continuing into the system of microscopic tubules where the composition of urine will be adjusted to the current needs of the organism. Once urine passes to the renal pelvis it cannot be adjusted anymore.

The **proximal convoluted tubule** detaches from the capsular space and continues in a "convoluted way" until it becomes the **loop of Henle**. From the loop of Henle, the filtrate continues to the **distal convoluted tubule** and then the **collecting duct**. The distal part of the collecting duct, called the **papillary duct**, releases urine to the renal pelvis.

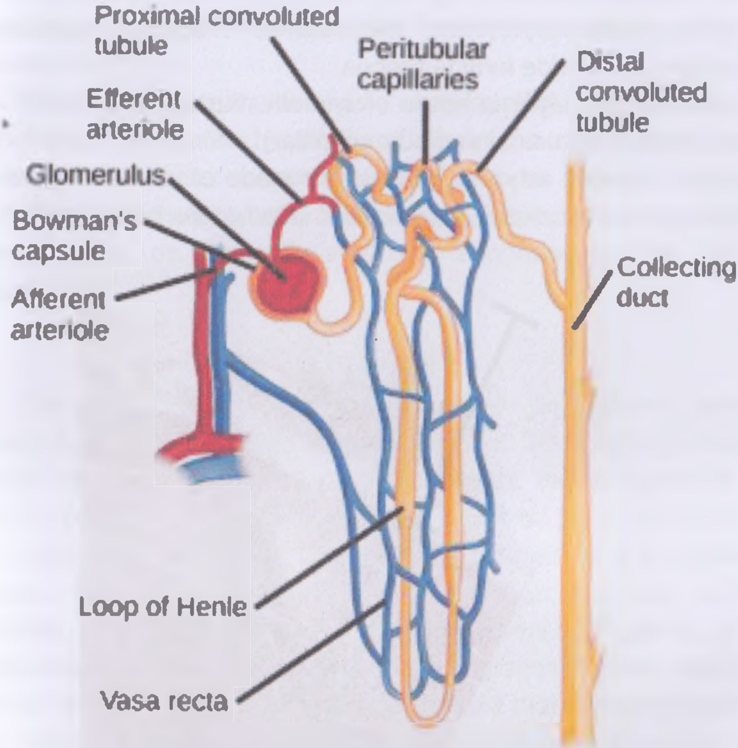


Fig. 44. Illustration indicating the parts of the nephron

All parts of the tubular system have a network of accompanying capillaries that pick up the substances that have been reabsorbed.

Below are the parts of the nephron listed in order of urine flow.

ORGANS OF URINE ELIMINATION

Once urine enters the renal pelvis, it will be delivered by the **ureters** to the **urinary bladder**, and then to the outside by the **urethra**. All organs for urine elimination are hollow with three-layered walls consisting of:

- mucosa;
- muscularis;

- adventitia.

The inside layer, **the mucosa**, is made of transitional epithelium and a wide lamina propria.

The **muscularis** layer is made of smooth muscle arranged in two layers (inner longitudinal and outer circular).

The outer layer is **adventitia,** which is made of connective tissue, and wherever it touches **peritoneum** it is called **serosa.**

Fig. 45. Three layers of the urinary bladder wall:
1. Mucosa; 2. Muscularis; 3. Adventitia

Transitional epithelium is multi-layered but lacks the organization of stratified epithelia. Cells in the upper layers have polyhedral shapes, becoming cuboidal in deeper regions, Transitional epithelium cells can change shape, in extreme cases becoming flat, as the walls stretch to accommodate the flow of stored urine.

Transitional epithelium is multi-layered but lacks the organization of stratified epithelia. Cells in the upper layers have polyhedral shapes, becoming cuboidal in deeper regions. Transitional epithelium cells can change shape, in extreme cases becoming flat, as the walls stretch to accommodate the flow of stored urine.

TRACHEA

The trachea connects the larynx above and the two primary bronchi below. The trachea is easily identified by its large C-shaped hyaline cartilage rings. These rings prevent the collapse of the tracheal mucosa during inspiration and reside on the anterior side of the trachea. The ends of the rings are bridged by the trachealis muscle, which is composed of smooth muscle fibers, on the posterior side of the trachea. Note the presence of glands in the submucosal layer of the trachea. These glands contain cells that secrete mucous and others that secrete fluid that is roughly isotonic with plasma. The fluid is released onto the surface of the epithelium. The epithelium in the trachea is pseudostratified.

The image below shows in higher magnification the components found in the wall of the trachea and large bronchi. The epithelium facing the lumen of the trachea is clearly pseudostratified with cilia and is discussed in more detail below. The epithelium rests atop a thick basement membrane. Beneath the basement membrane is the lamina propria that contains connective tissue and blood vessels. The epithelium, basement membrane and lamina propria compose the mucosal layer.

The submucosa resides below the mucosa and contains a large number of seromucinous glands. The glands secrete fluid and mucus onto the surface of the epithelium. The vapor from the fluid on the epithelium moistens the air which will help prevent desiccation in the alveoli when the air reaches that point. Note also the hyaline cartilage in the submucosa. In the trachea, the cartilage forms a C-shaped ring on the anterior side of the trachea. In bronchi, the cartilage forms plates.

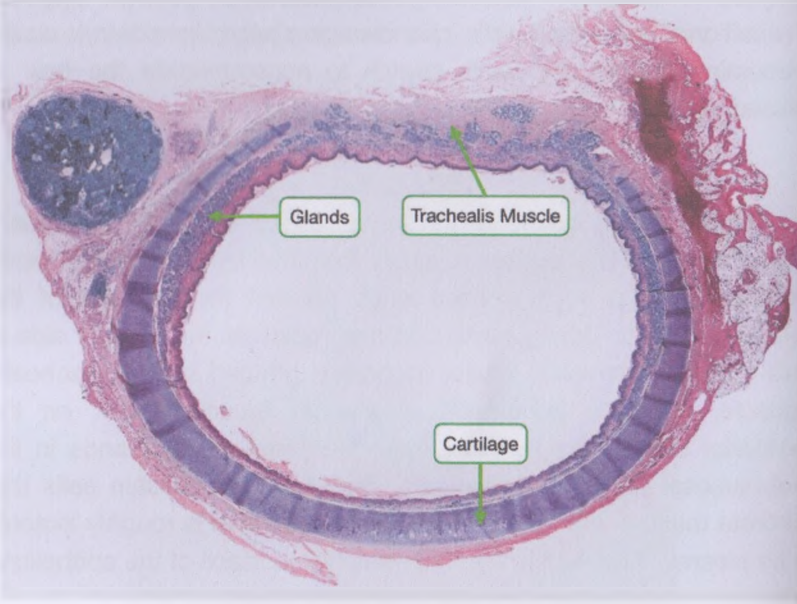


Fig. 46. Trachea

RESPIRATORY AIRWAYS

The respiratory airways extend from the respiratory bronchioles to the alveoli. The primary function of this section of the respiratory tract is to facilitate gas exchange.

Each respiratory bronchiole branches into 2 to 11 alveolar ducts that retain a cuboidal epithelium and still contain smooth muscle fibers in their walls. Along the walls of alveolar ducts are single alveoli and numerous alveolar sacs that comprise 2 to 4 alveoli. The space at the entrance from the alveolar duct to an alveolar sac is referred to as the atrium.

The epithelium of respiratory bronchioles is cuboidal with a mix of ciliated cells and club cells. Club cells perform several important functions, including production of material similar to surfactant, detoxification of inhaled chemicals, and absorption of ions and water from the airway lumen to control the amount of fluid in the airway. Club cells also serve as stem cells that are capable of replacing the other epithelial cells in respiratory bronchioles.

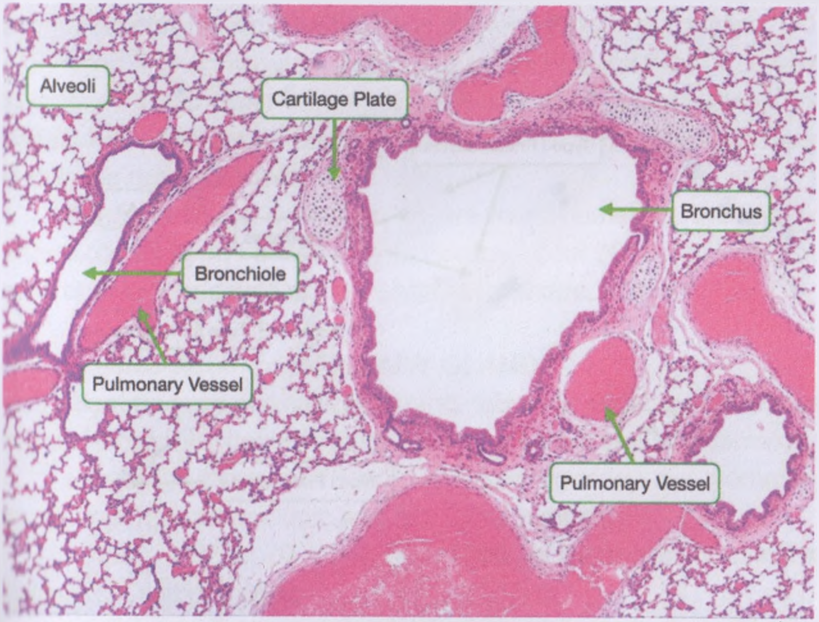


Fig. 47. Lung Section

Alveoli facilitate the exchange of gases between inhaled air and blood by creating a thin tissue layer between air and blood. The tissue layer consists of the airway epithelium, basement membrane and endothelium of the capillary. The combination of thin barrier between air and blood and large alveolar surface area allows for rapid diffusion of gases between air and blood.

Alveoli contain several different cell types which can be divided into resident cells and transient cells. Resident cells are those that create the structure of alveoli and participate in gas exchange. Resident cells include pneumocytes, endothelial cells and the occasional fibroblast. Transient cells include dust cells (macrophages) and other immune cells that vary in number depending on the presence of infectious agents and foreign particles.

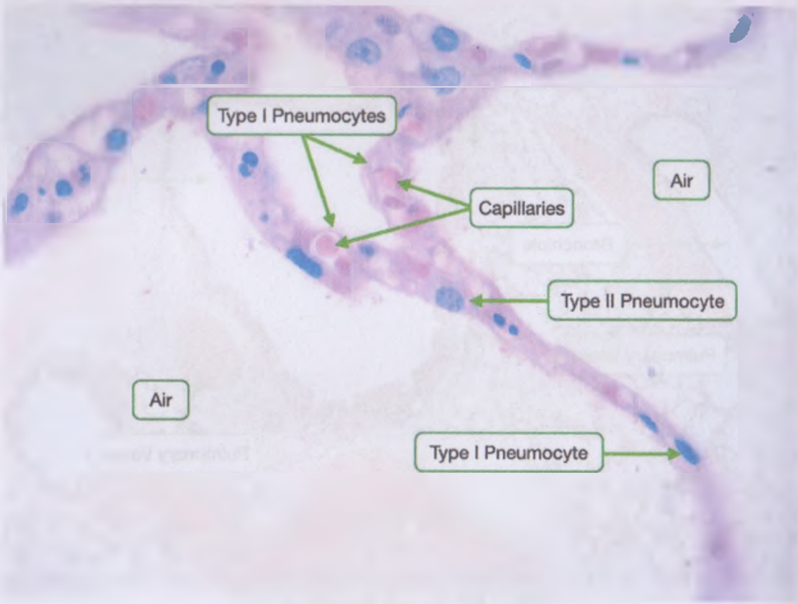


Fig. 48. Type pneumocytes

The surface (air-facing) epithelium of the alveoli contains two developmentally related but functionally distinct cells, known as pneumocytes. Type I pneumocytes form a simple, squamous epithelium that cover the vast majority of the surface area of alveoli. Type I pneumocytes surround a basement membrane and endothelial cells of capillaries to form the air-blood barrier, across which gases diffuse between air and blood.

Type II pneumocytes are larger, cuboidal cells. They produce and secrete surfactant into the fluid that faces the air space. Surfactant reduces the surface tension along the fluid-air boundary, preventing alveoli from collapsing. Surfactant contains molecules similar to lipids in that they contain hydrophilic and hydrophobic domains (amphiphilic). The hydrophobic domains interact with air while the hydrophilic domains associate with the fluid. Surfactant also contains protein components that function in innate immunity in addition to playing structural roles in the formation of surfactant.

Type II pneumocytes are often found in the junctions between to alveolar walls. After damage to alveoli, type II pneumocytes are capable of proliferating and differentiating into type I pneumocytes during the repair process.

Although type II pneumocytes are more numerous than type I pneumocytes, type I pneumocytes occupy about 95% of the surface area of alveoli because of their squamous shape.

MAMMARY GLAND

Mammary glands are compound, tubulo-alveolar glands whose structure changes depending on the reproductive status of females.

Lactating Mammary Gland – during pregnancy the mammary gland undergo morphologic and functional maturation.

Lobes – 15 to 20 lobes separated by septae of connective tissue with adipose cells.

Lactiferous Duct – each lobe is drained by a single lactiferous duct that opens into the nipple. It is lined by a double layer of cuboidal or columnar cells surrounded by a sheath of connective tissue with myoid cells.

Lobules – enclosed by a thin layer of connective tissue.

Intralobular Ducts – lined by one or two layers of cuboidal cells surrounded by a thin layer of connective tissue.

Terminal Ductules – branches of intralobular ducts lined with cuboidal secretory cells.

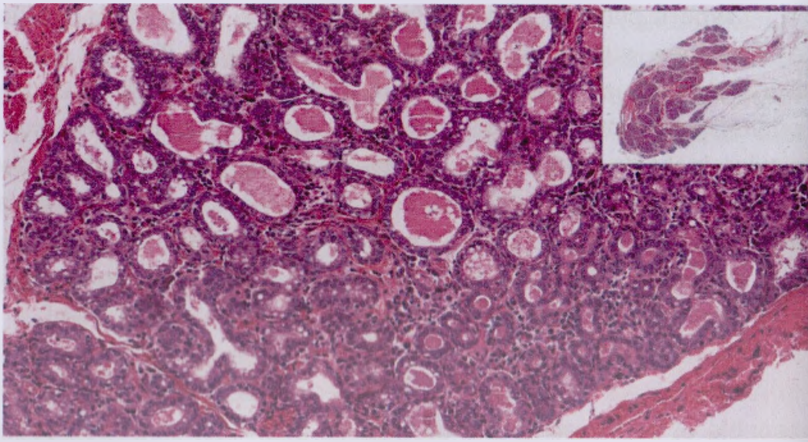


Fig. 49. Mammary gland

During pregnancy, they differentiate into secretory alveoli that produce milk.

Fig. 50. Mammary glands

Alveoli – grow and expand during pregnancy and lactation.
Simple Epithelium – cuboidal or columnar secretory cells that synthesis and secrete milk.

Milk – the eosinophilic material within the alveolar lumen and ducts is proteins from secreted milk.

Intralobular Stroma – loose connective tissue with few adipose cells.

HEART

The **heart** is a pump that contracts rhythmically sending blood through the cardiovascular system. The contractile wall of the heart, the myocardium, is composed of cardiac muscle cells.

The heart consists of four chambers: two **atria** and two **ventricles**. The atria receive blood, while the ventricles discharge blood from the heart.

Heart valves are thin folds of the endocardium with a core of dense connective tissue. To maintain their shape, heart valves are attached around the fibrous rings of the **cardiac skeleton**.

Purkinje fibers are specialized muscle fibers that relay impulses to create synchronized contractions of the ventricles.

Cardiac muscle (myocardium) is striated, involuntary muscle found in the heart wall. Cardiac muscle cells (cardiomyocytes) contain the same contractile filaments as in skeletal muscle (sarcomeres). They are intermediate in size compared to skeletal and smooth muscle.

Cross-Section – cardiac muscle cells have rounded cross-sections with a centrally located nucleus

Longitudinal Section - cardiac muscle cells are joined end-to-end are often branched

Nuclei – cardiac muscle cells have a single or occasionally two centrally located nuclei.

Intercalated Discs – cardiac muscle cells are joined together by specialized junctions called intercalated discs. They appear as thin, dark stained linear structures dividing adjacent cells that are perpendicular to the direction of the muscle fiber

Lipofuscin Pigment – residue of lysosomal digestion that accumulates as yellow-brown granules near the nucleus of some cells. In this specimen, few cells have detectable amounts.

Unlike skeletal muscle that is composed of a long row of cells with fused cytoplasm, cardiac muscle is composed of multiple branching cells that are joined by specialized structures, including intercalated discs. These appear as very fine lines between the cardiomyocytes.

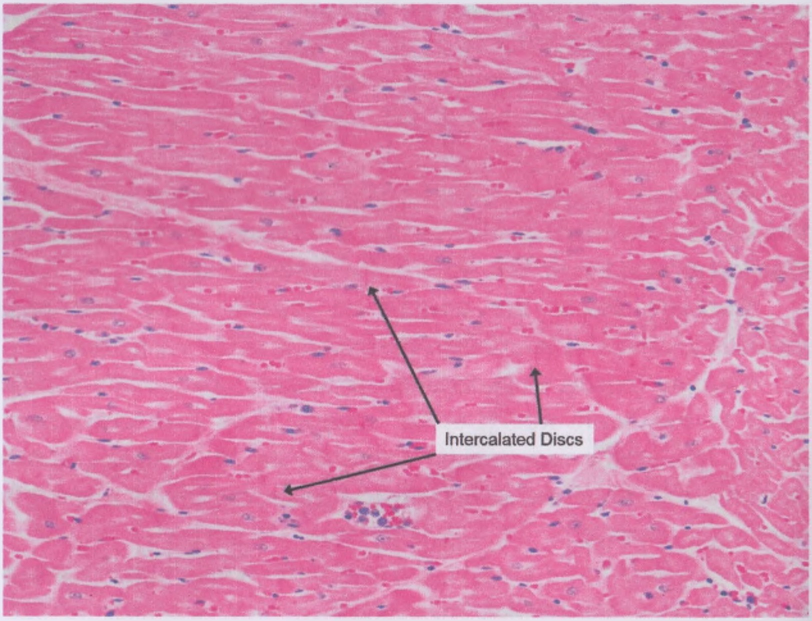


Fig. 51. Cardiac muscle.

CEREBRAL CORTEX

Unlike the highly organized cerebellar cortex, the cerebral cortex appears to be less well-organized when viewed with the light microscope. Nonetheless, it is loosely stratified into layers containing scattered nuclei of both neurons and glial cells.

Typically, one or more sulci (infoldings) will extend inward from one edge of the section. Examine the gray matter on each side of the sulcus using first low and then high power. Neurons of the cerebral cortex are of varying shapes and sizes, but the most obvious are pyramidal cells. As the name implies, the cell body is shaped somewhat like a pyramid, with a large, branching dendrite extending from the apex of the pyramid toward the cortical surface, and with an axon extending downward from the base of the pyramid. In addition to pyramidal cells, other nuclei seen in these sections may belong to other neurons or to glial cells also present in the cortex. You may be able to see subtle differences in the distribution of cell types in rather loosely demarcated layers. There are 6 classically recognized layers of the cortex:

1. Outer plexiform (molecular) layer: sparse neurons and glia.
2. Outer granular layer: small pyramidal and stellate neurons.
3. Outer pyramidal layer: moderate sized pyramidal neurons.
4. Inner granular layer: densely packed stellate neurons (usually the numerous processes are not visible, but there are lots of nuclei reflecting the cell density).
5. Ganglionic or inner pyramidal layer: large pyramidal neurons.
6. Multiform cell layer: mixture of small pyramidal and stellate neurons.

Throughout each of these layers are a large variety of inhibitory interneurons that vary in size and morphology. The vast majority of these interneurons are small with cell bodies that are typically smaller than the pyramidal neurons in layer V and axons that only project locally within a few millimeters of their origins in the cerebral cortex.

Pyramidal cells in layers III and V tend to be larger because their axons contribute to efferent projections that extend to other regions of the CNS –pyramidal neurons in layer V of motor cortices send projections all the way down to motor neurons in the spinal cord! Of those that are neurons, roughly half are excitatory (pyramidal, stellate and semilunar neurons) and the other half are inhibitory interneurons. Deep to the gray matter of the cerebral cortex is the white matter that conveys myelinated fibers between different parts of the cortex and other regions of the CNS.

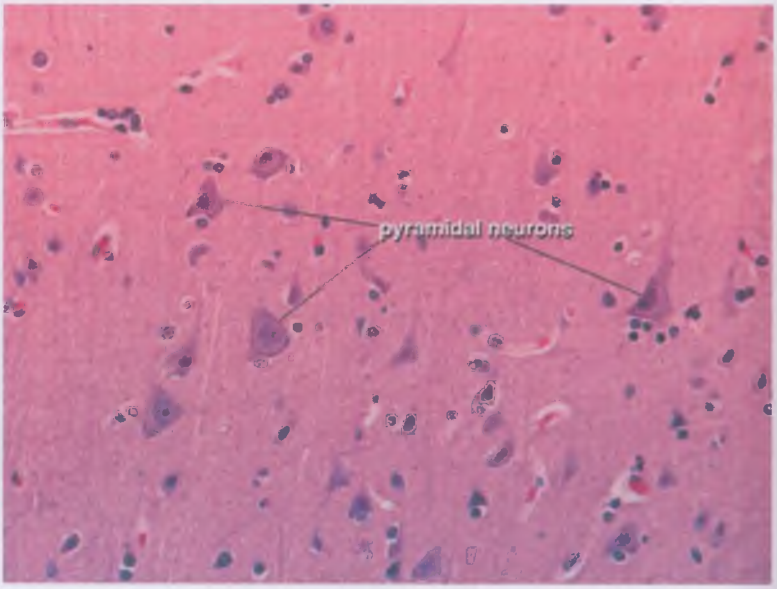


Fig. 52. Pyramidal cells

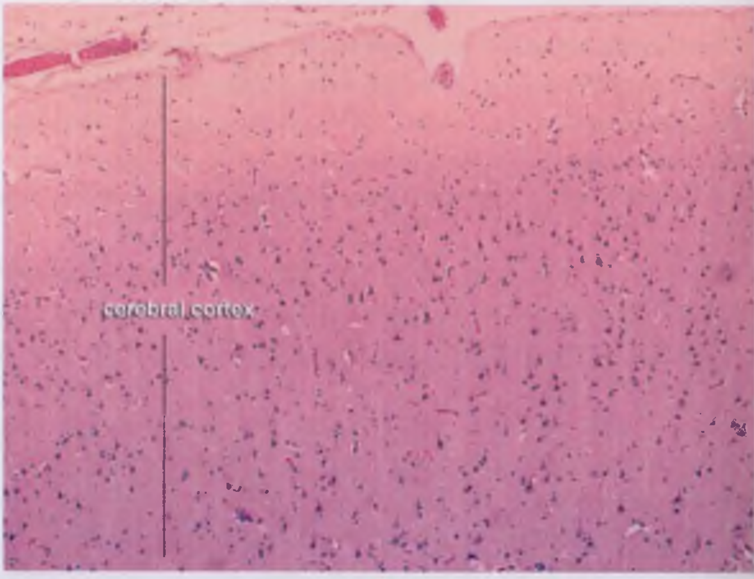


Fig. 53. Cerebellar cortex

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