2024

Virtual Microscopy
Histology and Histopathology

TRAINING GUIDE

ON ADVANCED VIRTUAL MICROSCOPY IN HISTOLOGY AND HISTOPATHOLOGY

Co-funded by
the European Union

Digital transformation of Histology and Histopathology by Virtual Microscopy (VM) for an innovative medical school curriculum

ERASMUS+ PROJECT, REF.NO. 2022-1-RO01-KA220-HED-000089017

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Virtual Microscopy
Histology and Histopathology

Course Overview

The Training Course on Advanced Virtual Microscopy (VM) in Histology and Histopathology is designed to modernize microscopy education by integrating digital tools into the teaching and learning process. This course provides a comprehensive and practical guide to implementing VM technology in medical schools, ensuring cost-effective solutions for digital transformation.

Aims of the Course

- To harmonize microscopy education across European medical institutions, reducing disparities in histology and histopathology curricula.
- To equip educators with the necessary skills to implement and utilize VM technology effectively in their teaching.
- To create a structured, multilingual training guide that supports digital transformation in microscopy education.
- To develop digital readiness, resilience, and capacity in histology and histopathology teaching.

Target Group

This training course is designed for:

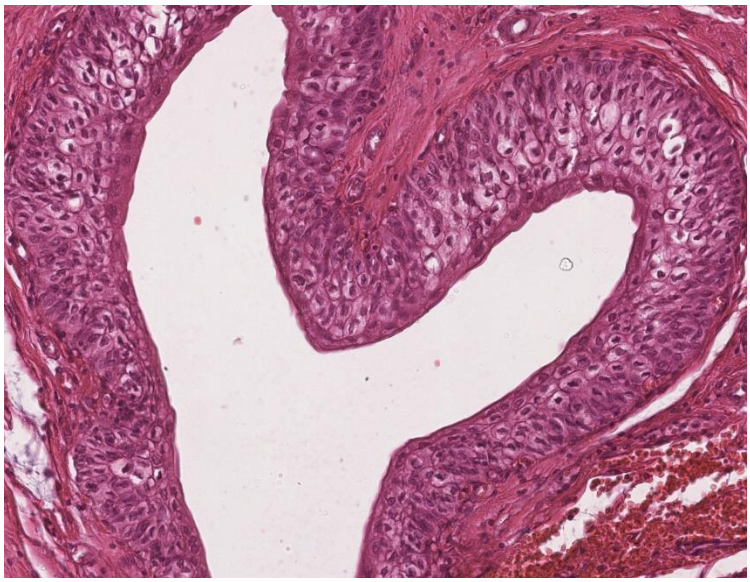
- Teaching staff in histology and histopathology departments across European universities.
- Medical educators looking to implement digital microscopy in their curricula.
- Undergraduate and postgraduate medical students seeking a modernized approach to microscopy education.

Learning Objectives

By the end of this course, trainees will be able to:

- Explain the principles and advantages of VM in histology and histopathology education.
- Identify the technical requirements and implementation strategies for VM in medical curricula.
- Navigate and utilize digital slides effectively for teaching and self-learning.
- Recognize and differentiate various tissue types and pathological conditions using VM.
- Interpret histological and histopathological features in digital slides.
- Reflect on personal learning progress and identify areas for improvement.
- Identify and differentiate basic tissue types, including epithelial, connective, muscular, and nervous tissues.
- Recognize the structural organization of organs and systems at the microscopic level.
- Describe histological variations in different physiological and pathological conditions.
- Correlate microscopic structures with their functions in normal and diseased states.
- Distinguish between normal and abnormal histological features.
- Recognize key histopathological changes associated with major diseases.
- Interpret digital histological slides to identify pathological conditions.
- Utilize VM to analyze complex cases requiring special staining techniques.

CHAPTER 1 - Epithelial tissue



Epithelial tissue is a fundamental tissue that serves as a protective barrier, participates in absorption, secretion, and sensory perception, and plays critical roles in tissue homeostasis. Epithelium functions are supported by a variety of specializations, like cilia, microvilli, and secretory organelles, as well as a network of junctions that ensure structural integrity and coordination between cells. Epithelial cells are tightly packed together and are connected by specialized junctions that provide strength, communication, and selective permeability, as occluding junctions, anchoring junctions, and communicating junctions.

Epithelial tissue is classified into two main types based on its function: lining epithelial tissue and glandular epithelial tissue. Lining epithelial tissue forms continuous sheets that cover the external surfaces of the body (like the skin) and line the internal cavities, organs, and ducts. Additionally, lining epithelial tissue is classified based on two main criteria: the number of cell layers and the shape of the cells. These criteria may lead to classification into different types of epithelial tissue, each suited to specific functions. According to the number of cells layers, there are two types of epithelia: simple epithelium, with a single layer of squamous, cuboidal or columnar cells, and stratified epithelium, with multiple layers of cells. The superficial layer of cells in stratified epithelia may be also squamous, cuboidal or columnar. Moreover, the squamous superficial cells may be keratinized, as in the epidermis of the skin or non-keratinized, as in the esophagus. Transitional epithelium is a particular stratified epithelium, able to stretch, which can be found in the urinary tract. Pseudostratified epithelium appears as layered but is composed of a single layer of cells of varying heights, often ciliated, found in the respiratory tract.

Epithelial cells are characterized by apical-basal polarity, with distinct structural and functional properties for the different regions of the cells. The basement membrane provides structural support, anchors epithelial cells to the underlying connective tissue, and regulates cell behaviour. It consists of two layers: basal lamina (produced by epithelial cells) and reticular lamina (produced by connective tissue). On the basement membrane, there are stem cells that can self-renew and differentiate into various cell types.

Glandular epithelium is specializing in secretion and forms the glands of the body. It can be divided into two main types: exocrine and endocrine. The exocrine glands are composed by a secretory portion and ducts, while endocrine glands are composed only of secretory component, disposed in cords, with only one exception, which displays a follicular pattern (thyroid gland).

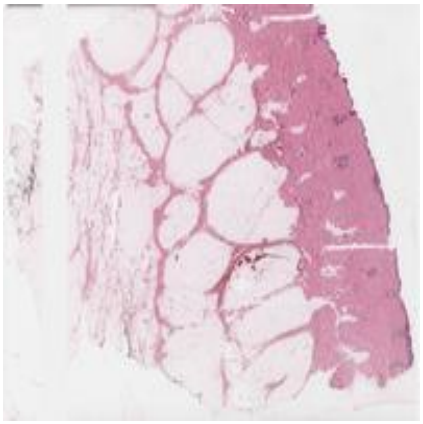
This virtual library section illustrates the histological features of the lining and the glandular epithelial tissue, as a first step in understanding the histopathological features of the non-tumoral and tumoral lesions that involve the epithelial tissue. Epithelial tissues are often the first line of defence against pathogens and toxins, so they are heavily involved in the immune response. Many cancers originate from epithelial cells, being named carcinomas.

Epithelial tissue research is progressing rapidly, driven by advancements in molecular biology, tissue engineering, and regenerative medicine, guided by the efforts made to understand many diseases, particularly cancer, added to inflammatory and degenerative diseases.

1.1 Simple squamous epithelium - endothelium - Jejunum submucosa

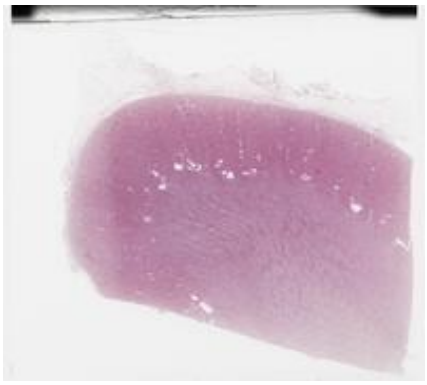
The slide shows a section of jejunum, composed of mucosa, submucosa, muscularis externa, and serosa, to exemplify a type of simple epithelium, in its submucosa layer. Simple epithelium has only one cell layer, where every cell is in direct contact with the underlying basement membrane. Squamous epithelial cells are planar thin cells. Being a thin layer, it has the physiological advantage of faster absorption and filtration. In the submucosa region of the jejunum, several blood vessels transport the nutrients obtained in absorption. The endothelium is a type of simple squamous epithelium found on the inner surface of lymphatic and blood vessels. The endothelial cells that line the vessel are squamous cells. Nervous fibers together with ganglion cells, belonging to submucosal (Meissner's) plexus are also visible.

1.2 Simple squamous epithelium - endothelium - Papillary dermis



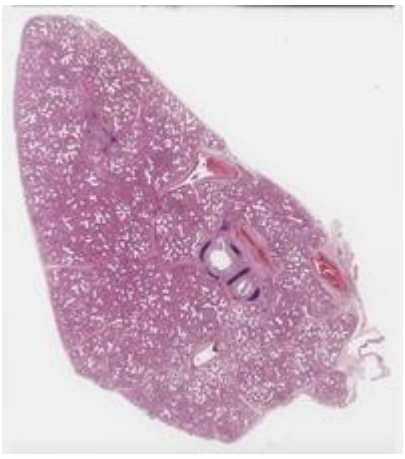
The slide shows a section of tegument, composed of thin epidermis, dermis, and underlying hypodermis, to exemplify a type of simple epithelium in its dermis. The most external layer is epidermis (keratinized stratified squamous epithelium). The underlying layer, the dermis, is a connective tissue. The upper part of the dermis is called the papillary dermis, containing blood vessels (capillary loops) to provide nutrients and oxygen to the epidermis and to control the skin's temperature. The endothelial cells that line the vessels are planar thin cells (squamous cells), arranged in a single cell layer, where every cell is in direct contact with the underlying basement membrane (simple squamous epithelium), with the physiological advantage of faster absorption and filtration.

1.3 Simple squamous epithelium - Bowman's capsule outer parietal layer – Kidney



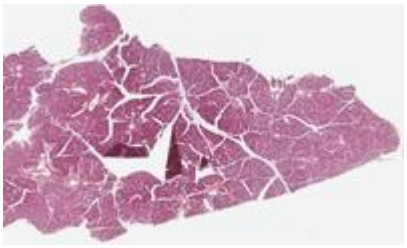
The slide shows a section of kidney, consisting of cortex, medulla and pelvis, to exemplify a type of epithelium in its cortex. The renal cortex is the outer layer of the kidney tissue and contains renal corpuscles and coiled tubules of the nephrons. The renal corpuscle is the filtration apparatus of the nephron. Each corpuscle has two main elements: the glomerulus and glomerular (Bowman's) capsule. The outer parietal layer of the Bowman's capsule is made up of simple squamous epithelium, while the inner visceral layer is made up of podocytes. Squamous epithelial cells are planar thin cells, disposed in only one cell layer, where every cell is in direct contact with the underlying basement membrane, as seen in the outer parietal layer of Bowman's capsule.

1.4 Simple squamous epithelium - Mesothelium - Fetal lung



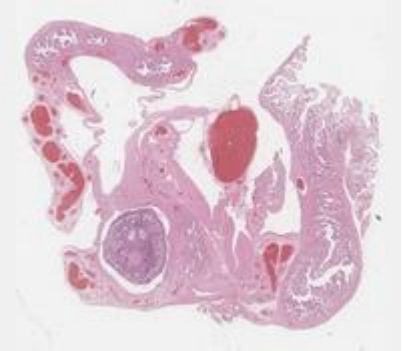
The slide contains a section of a fetal lung, to exemplify mesothelium. The lung contains potential small air spaces, almost completely lined by a low cuboidal epithelium and separated from one another by broad cellular walls. There are also developing bronchi and developing bronchioles, along with respiratory components, with alveolar ducts, sacs, and alveoli. The bronchi associated lymphatic tissue (BALT) is well represented. The layer surounding the organ is the visceral pleura, composed of reduced connective tissue covered by a simple squamous epithelium layer, named mesothelium.

1.5 Simple cuboidal epithelium - Ducts - Mixed salivary gland



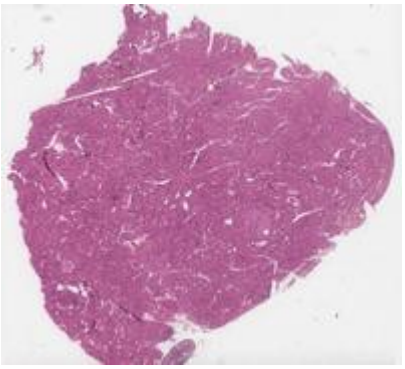
The slide shows a mixed salivary gland, to exemplify simple cuboidal epithelium lining some type of ducts. The simple epithelium has only one cell layer, where every cell is in direct contact with the underlying basement membrane. Cuboidal epithelial cells are shaped like a square or cube, with their spherical nuclei in the center. The salivary glands are exocrine glands responsible for the production and secretion of saliva. The secretory cells are organized into secretory units (acini), small gland-like structures of three types (serous, mucous, and mixed) that empty into branched intralobular circuits as well as into extralobular ducts. Intralobular ducts may be lined by simple cuboidal epithelium (intercalated ducts) and by simple columnar epithelium (striated ducts).

1.6 Simple cuboidal epithelium - Germinal epithelium - Ovary surface



The slide shows a section of ovary, to exemplify simple cuboidal epithelium covering its surface. The ovary is a small almond shaped structure in which ooctyes develop, within primordial, growing, and mature (Graafian) ovarian follicles, and female sex hormones are produced. The ovaries are covered by a protective epithelium, a layer of simple cuboidal epithelium, called germinal (ovarian) epithelium. This simple epithelium has only one cell layer, where every cell is in direct contact with the underlying basement membrane and their shape is cuboidal, with their spherical nuclei in the cell center.

1.7 Simple cuboidal epithelium - Thyrocytes / Follicular cells – Thyroid

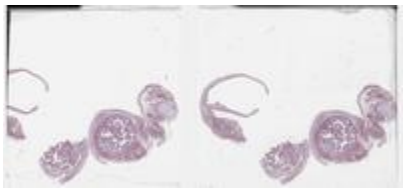


The slide shows a section of thyroid, to exemplify simple cuboidal epithelium lining the thyroid follicles. The thyroid gland is an endocrine gland, encased by a thin connective tissue capsule that send septa that subdivide the gland into irregular lobular units. Each lobule contains a cluster of follicles, which are the structural and functional units of the thyroid gland. The cells that line each follicle are called thyrocytes or follicular cells, as an example of a simple cuboidal epithelium. This simple epithelium has only one cell layer, where every cell is in direct contact with the underlying basement membrane, while the epithelial cells are shaped like squares or cubes, with their spherical nuclei in the cell center.

1.8 Simple cuboidal epithelium - Tubules – Kidney

The slide shows a section of a kidney, to exemplify simple cuboidal epithelium lining nephron's tubules. The kidneys are paired retroperitoneal organs of the urinary system. Each kidney consists of a cortex, medulla, and pelvis. The nephrons, functional filtration units, extend through the cortex and the medulla regions. While a simple squamous epithelium forms the outer parietal layer of glomerular (Bowman's) capsule and the loop of Henle thin descending and thin ascending limbs, the other tubules of the nephron are lined by simple cuboidal epitheliums. These structures include the proximal convoluted tubule close to the glomerulus in the cortex, the proximal straight segment which enters the medulla region, the straight distal tubule (thick ascending limb), between the inner and outer medulla, and the convoluted distal tubule which projects into the cortex. The simple epithelium lining the tubules has only one cell layer, where every cell is in direct contact with the underlying basement membrane, while the cells are shaped like squares or cubes, with their spherical nuclei in the cell center. A pivotal difference in distinguishing between the proximal and distal tubules is that the epithelium of the distal tubule has less well-developed microvilli.

1.9 Simple columnar epithelium - Fallopian tube



The slide shows a section of the fallopian tube (uterine tubes or oviducts) to exemplify simple columnar epithelium. Columnar epithelial cells are tall and narrow, giving them a column-like appearance, with oval-shaped nuclei located in the basal region, disposed in only one cell layer, with all the cells in direct contact with the underlying basement membrane. The fallopian tubes connect the peritoneal cavity, close to the ovaries, with the uterine cavity, being composed of mucosa, muscularis, and serosa. They provide a site for fertilization and are involved in the transport of the oocytes from the ovaries to the body of the uterus. The lumen of the fallopian tube is lined by a simple columnar epithelium. Most columnar epithelial cells of oviducts are ciliated columnar cells, but we can also distinguish secretory (peg) cells and intercalated non-ciliated cells.

1.10 Simple columnar epithelium - Gastric epithelium

The slide shows a section of gastric (fundic) region of the stomach, to exemplify simple columnar epithelium. The stomach is an organ of the digestive system, specialized in the accumulation and digestion of food, being composed of four layers. The internal surface of the stomach has a wrinkled aspect consisting of ridges called gastric folds or rugae, composed of mucosa and submucosa. A simple columnar epithelium lines the mucosa, with only one cell layer, where every cell is in direct contact with the underlying basement membrane, made up of tall and narrow cells, with a column-like appearance and oval-shaped nuclei located in the basal region. The epithelial layer contains numerous invaginations, called gastric pits, while gastric glands (fundic or cardiac or pyloric) open into their bottom. The epithelial columnar cells of the surface are called surface mucous cells or foveolar cells and are covered by a protective, alkaline mucous layer. The apical part of these cells contains cytoplasmic neutral mucins, showing a lightly eosinophilic apical mucin cap.

1.11 Simple columnar epithelium - Intestinal epithelium – Jejunum

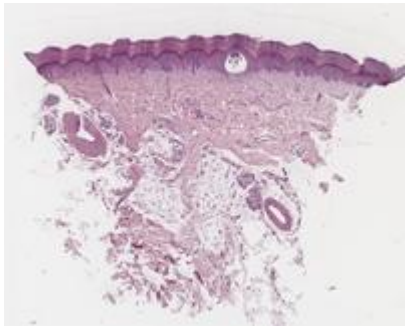
The slide shows a section of jejunum, to exemplify simple columnar epithelium. Jejunum has four layers: mucosa, submucosa, muscularis propria (muscularis externa), and serosa. Mucosa consists of simple columnar epithelium, with intestinal villi and intestinal glands (Lieberkühn crypts), lined by enterocytes and goblet cells, lamina propria (loose connective tissue), and muscularis mucosae. The simple epithelium lining the villi and crypts has only one cell layer, where every cell is in direct contact with the underlying basement membrane, while all epithelial cells are tall and narrow, giving them a column-like appearance, with oval-shaped nuclei located in the basal region. The submucosa is a layer of connective tissue containing blood vessels, lymphatic vessels, and

nerves. The muscularis externa consists of two layers of smooth muscle: an inner circular layer and an outer longitudinal layer. Serosa is composed of connective tissue and mesothelium.

1.12 Pseudostratified epithelium - respiratory type – Trachea

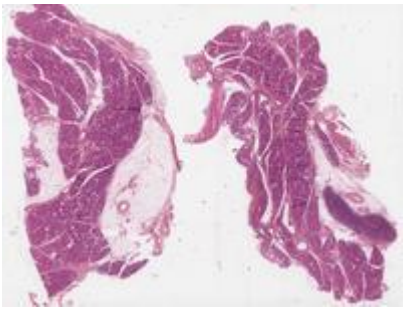
The slide shows a section of trachea, to exemplify pseudostratified epithelium of respiratory type. Pseudostratified epithelium, also called respiratory epithelium, since it lines the respiratory tract, has a false multilayered appearance due to different height of its cells and the disposition of the cell nuclei at different levels, respectively, but actually each cell rests on a thick basement membrane and not all of them reach the apical surface. The basement membrane separates the epithelium from the underlying connective tissue. Cells exhibit polarity with typical localization of the nuclei in the basal two-thirds of the epithelium. The columnar cells bear cilia, which extend from the apical surface of the cells. Between the columnar ciliated cells, there are goblet cells that secrete mucus and basal cells that undergo mitosis to replace the other types of cells of this epithelium. The main functions of pseudostratified columnar epithelium are protection, secretion, and mucus movement.

1.13 Stratified cuboidal epithelium - Ducts of sweat glands – Skin



The slide represents a section of the skin lined by thick epidermis, which is found on the palms of the hands and the soles of the feet. The epidermis is supported by dermis and hypodermis. The thick epidermis layers are: stratum basale (basal layer), stratum spinosum, stratum granulosum (granular layer), stratum lucidum, and stratum corneum (cornosum layer). Dermis is a connective tissue that supports the epidermis, composed of dermal papillae, with loose connective tissue, rich in capillaries and reticular (deep) dermis, made up of dense irregular connective tissue, containing skin adnexa. The skin adnexa seen in this type of skin are eccrine sweat glands, as coiled tubular glands, with lightly stained secretory portions. Their ducts are darkly stained and are lined by two layers of cells, cuboidal basal layer and superficial cuboidal layer, both exhibiting round nuclei, forming a bistratified cuboidal epithelium.

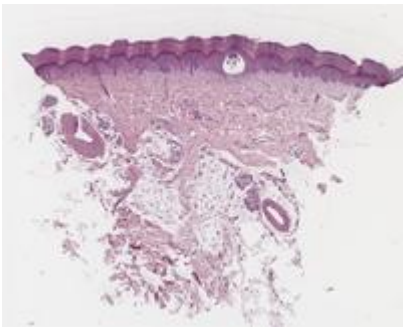
1.14 Stratified columnar epithelium - Ducts – Parotid



The slide shows a major pure serous salivary gland (parotid), to exemplify stratified columnar epithelium. The gland is surrounded by a dense irregular connective tissue capsule, sending septa that divide the gland into lobules and contains a loose connective tissue stroma, associated with white adipose cells. Parenchyma consists of secretory cells disposed in serous acini. Intralobular ducts are intercalated ducts and striated ducts. Interlobular (extralobular or excretory ducts) are disposed in the connective tissue septa and are lined by

pseudostratified, stratified cuboidal or stratified columnar epithelium (basal cuboidal cells, superficial columnar cells, and variable interposed cells).

1.15 Stratified squamous epithelium keratinized - Skin with thick epidermis



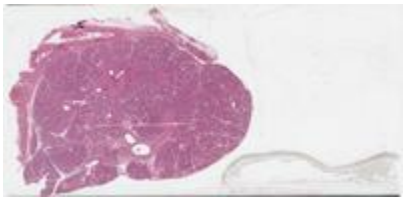
The skin is the largest human organ and has a variety of functions, including mechanical protection and sensory function. The slide is a section of so-called "thick skin" or skin with thick epidermis, which is mainly found on the palms of the hands and the soles of the feet. Skin epithelium is a keratinized stratified squamous epithelium that consists of five layers: the stratum germinativum, stratum spinosum, stratum granulosum, stratum lucidum, which is difficult to see, and stratum corneum, from basal to apical location. The basal layer is composed of cuboidal stem cells with high mitotic activity. These cells migrate towards the surface, forming the different layers of the epidermis, until they reach the last layer formed by keratin. The thick skin has a wide stratum corneum and its underlying dermis contains eccrine sweat glands but lacks hair follicles and sebaceous glands.

The skin is the largest human organ and has a variety of functions, including mechanical protection and sensory function. The slide is a section of so-called "thin skin" (skin with thin epidermis), which is the most abundant skin type. It has a keratinized stratified squamous epithelium that consists of four layers: the stratum germinativum, stratum spinosum, stratum granulosum, and stratum corneum, from basal to apical location. The basal layer is composed of cuboidal stem cells with high mitotic activity. These cells migrate towards the surface, forming the different layers of the epidermis, until they reach the last layer formed by keratin. Thin skin has a slim stratum corneum and its underlying dermis contains sebaceous glands attached to hair follicles, as well as eccrine sweat glands.

1.16 Nonkeratinized stratified squamous epithelium – Esophagus

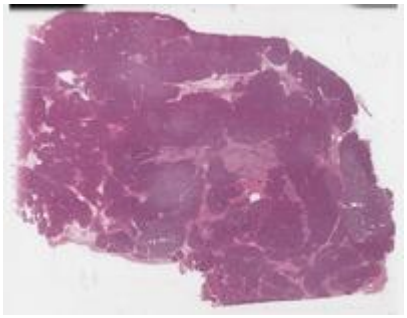
The slide shows a section of esophagus, the first segment of the digestive tube that carries food and other substances from the oropharynx to the stomach. This organ is composed of mucosa, submucosa, muscularis externa, and adventitia/serosa. The mucosa has a nonkeratinized stratified squamous epithelium where the new cells are produced in the basal layer. This layer is composed of cuboidal stem cells that migrate towards the surface, changing their shape, size, and nuclei location until they reach the most apical, superficial layer where cells become flattened (squamous) and are sloughed off into the esophageal lumen.

1.17 Glandular exocrine epithelium - Acini - Mixed - Mixed salivary glands



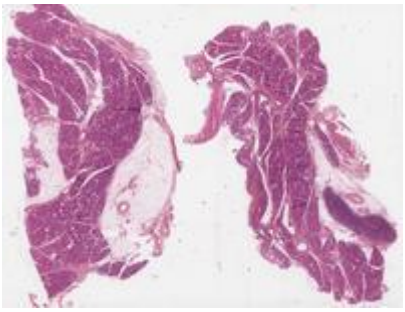
The slide shows a mixed salivary gland, to exemplify variable types of acini. Mixed salivary glands consists of a mixture of serous, mucous, and muco-serous (mixed) secretory units. Mucous acini stain poorly with H&E, in contrast to the serous ones. The mixed acini contain serous demilunes that surround mucous cells. The secretory units surround ducts lined by simple cuboidal epithelium that empty into a larger striated duct, lined by simple columnar epithelium, with striated basal cytoplasm. Myoepithelial cells are located closed to the basal lamina of secretory units (acini or adenomeres).

1.18 Glandular epithelium - Exocrine glands - Serous acini – Pancreas



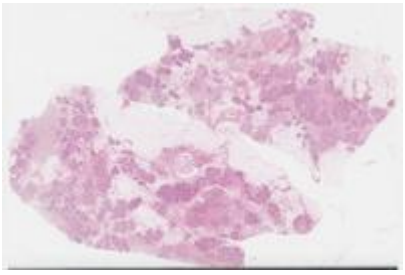
The slide shows a section of pancreas, to exemplify serous acini. The pancreas is a large gland with exocrine and endocrine functions. The exocrine component consists of an extensive tubuloacinar system that drains into a branched duct. Each acinus drains into a small duct (intercalated duct) lined by simple cuboidal epithelium that continue with intralobular and interlobular ducts that may be lined by stratified epithelium in the larger excretory ducts. Serous acini appear as more or less rounded structures with nuclei in the basal pole, surrounded by basophilic cytoplasm. The apices of the cells have eosinophilic and granular appearance. Generally, centroacinar cells, representing the initial portion of intercalated ducts, are identified in the centre of the acini.

1.19 Glandular epithelium - Exocrine glands - Serous acini - Parotid gland



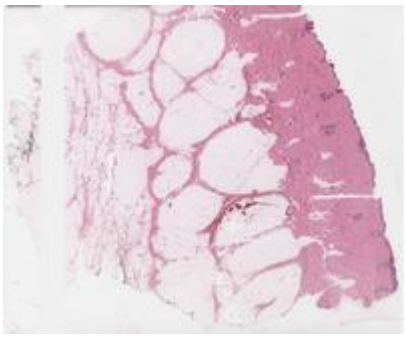
The slide shows a section of the parotid, a salivary gland that produces a watery secretion, being composed of serous acini. These have secretory cells with rounded nuclei in basal position and basophilic cytoplasm, containing proteins. The secretory units are associated with intercalated ducts lined by cuboidal epithelium that empty into larger striated ducts, lined by tall columnar cells in which the basal cytoplasm appears striated. A large amount of fat tissue (adipocytes) is usually present in the parotid gland, increasing in amount with age.

1.20 Glandular epithelium - Exocrine glands - Alveolar type - Mammary gland



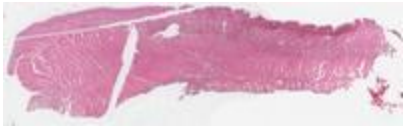
The slide shows a section of the mammary gland, a complex structure crucial for lactation. It consists of lobules, each containing intralobular ducts (terminal ductules or terminal duct lobular units), lined by simple cuboidal epithelium, associated with myoepithelial cells. During lactation, alveoli arise from terminal ductules, being lined by active secretory cells, which produce milk components. Myoepithelial cells are surrounding the alveoli, assisting the contraction of the alveoli for milk expulsion during breastfeeding. Lobules, formed by branched ducts ± alveoli, are organized into lobes connected by interlobular ducts, lined by simple columnar epithelium and collected into lactiferous sinus, lined by bistratified cuboidal epithelium, which transport milk towards the nipple. There is also a variable amount of white adipose tissue.

1.21 Glandular epithelium - Exocrine glands - Sebaceous gland – Skin



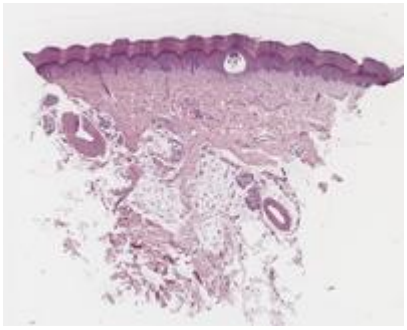
The slide shows a section of skin (integument), composed of thin epidermis, dermis with skin appendages, and underlying hypodermis, to exemplify sebaceous glands. These are acinar cutaneous glands generally associated with hair follicles. Each sebaceous gland has a branched acinar form, the acini converging upon a short duct which empties into the hair follicle. Each acinus is composed of rounded cells plenty of lipid vacuoles. As the cells approach to hair follicle, they enlarge and accumulate lipid droplets, their cell nuclei become increasingly pyknotic until the cell membranes rupture and release their contents, called sebum, into the pilosebaceous canal. This type of release of its content is called holocrine secretion. There are also basal, regenerative, cuboidal cells on the basement membrane. Arrector pili muscles surround the sebaceous glands.

1.22 Glandular epithelium - Exocrine glands - Tubular glands - Stomach fundic region



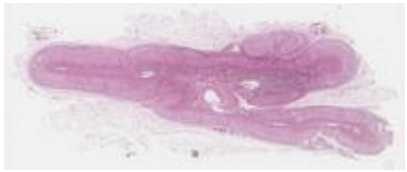
The slide shows a section of stomach fundic region, composed of mucosa, submucosa, muscularis externa, and serosa, to exemplify tubular glands. The gastric glands are located in the fundus and body of the stomach. They are branched tubular glands and are divided into three segments: isthmus, which contains the stem cells, neck, and fundus. The mucosa is lined by gastric pits, which are invaginations of the lining epithelium that branch out, being lined by surface mucous cells. The exocrine cells of the fundic glands are: mucous neck cells, parietal cells, which are eosinophilic, predominate in the isthmus and neck, and secrete hydrochloric acid and intrinsic factor, and chief cells, which are basophilic and secrete pepsinogen, being found mainly at the base of the glands. The endocrine cells are dispersed between exocrine cells.

1.23 Glandular epithelium - Exocrine glands - Simple coiled tubular glands - Sweat glands – Skin



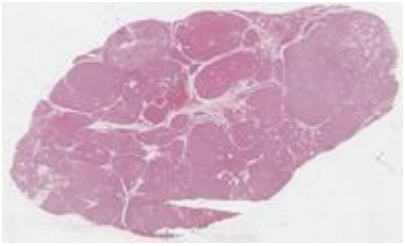
The slide represents a section of the skin lined by thick epidermis, which is found on the palms of the hands and the soles of the feet, to exemplify sweat glands, which are abundant in this location. The epidermis is supported by dermis and hypodermis. The thick epidermis layers are: basal, spinosum, granulosum, lucidum, and corneum. Dermis is a connective tissue that supports the epidermis, composed of dermal papillae, with loose connective tissue and reticular (deep) dermis. The skin adnexa seen in this type of skin are eccrine sweat glands, as coiled tubular glands, with lightly stained secretory portions (adenomeres), which secrete a watery fluid. The secretory components are lined by a simple cuboidal to columnar epithelium, with clear cells, dark cells, and myoepithelial cells, whereas the ducts are composed of bistratified cuboidal epithelium that extend through the epidermis and open directly onto the skin surface.

1.24 Glandular epithelium - Endocrine glands - Adrenal gland



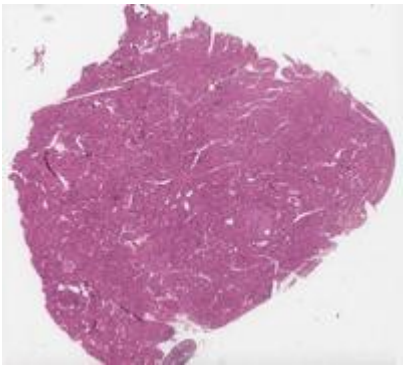
The slide shows a section of adrenal gland (suprarenal gland), which is a paired organ located in the retroperitoneal space of the abdominal cavity and exhibits a distinctive structure reflecting its function in the production of steroid hormones and catecholamines. The parenchyma, surrounded by a thick capsule of connective tissue, is organized into two main regions: cortex and medulla. The cortex consists of three distinct layers, each containing cells that produce different types of steroid hormones. Zona glomerulosa, located below the capsule, is composed of cylindrical or pyramidal cells arranged in arc-shaped cords. The cells in the next zone, beneath glomerulosa, zona fasciculata, are large, polyhedral, plenty of lipid droplets, and arranged in parallel cords. These cells have one or two lightly staining spherical nuclei. In the next zone, zona reticularis, the cells are smaller than in zona fasciculata, have fewer lipid droplets, and deeply stained nuclei. Cell cords of zona reticularis are organized in an anastomosing network and are rich in lipofuscin granules, in adults. The medulla, which forms the centre of the gland, is composed of polyhedral pale-staining cells, containing catecholamine granules, arranged in rounded cords or clusters, supported by a network of reticular fibres. These cells are called chromaffin cells.

1.25 Glandular epithelium - Endocrine glands – Parathyroid



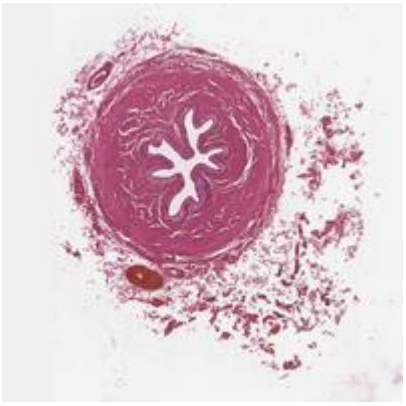
The slide shows a section of the parathyroid gland, which is surrounded by a capsule of connective tissue and is organized in lobules, which are typically composed of two main cell types: chief cells (principal cells) and oxyphil cells. Chief cells are the predominant cell type in the parathyroid gland and are responsible for the production and secretion of the parathyroid hormone. These cells are small and polygonal, have round central nuclei and pale eosinophilic or clear cytoplasm, plenty of glycogen and lipid droplets. Oxyphil cells are usually larger than chief cells, possess an eosinophilic cytoplasm, and their cell membranes are usually more evident.

1.26 Glandular epithelium - Endocrine glands - Follicular type – Thyroid



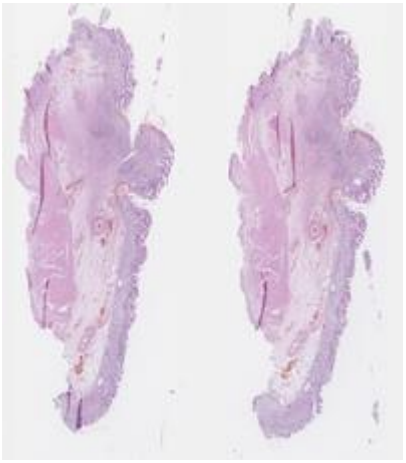
The slide shows a section of thyroid gland, which is surrounded by a capsule sending septa that divide the parenchyma into lobes and lobules, composed of follicles surrounded by connective tissue. Each follicle consists of a single layer of epithelial cells called follicular cells or thyrocytes. These cells form a simple cuboidal or low columnar epithelium with short microvilli and are arranged in a circular or irregular pattern around a central colloid-filled lumen. The colloid, secreted and resorbed by the follicular cells, is composed of thyroid hormone precursor, known as thyroglobulin. The colloid is a gel-like substance rich in thyroglobulin, which serves as the substrate for thyroid hormone production. Interspersed among the follicular cells or between follicles, there are also parafollicular cells, also known as C cells. These cells produce calcitonin, a hormone involved in calcium homeostasis, that is released directly into the connective tissue near capillaries.

1.27 Transitional epithelium – Ureter

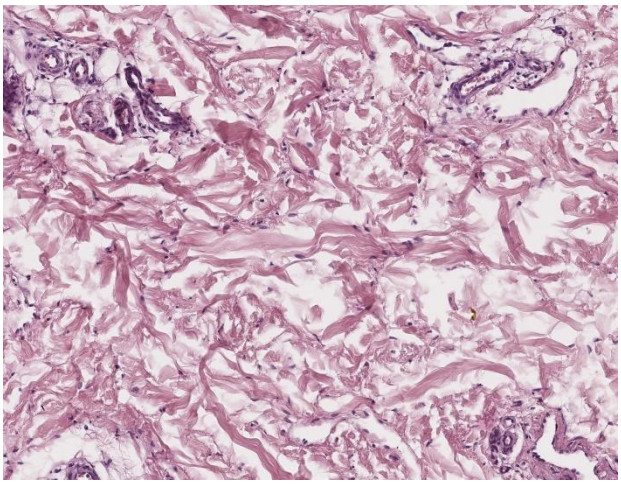


The slide shows a section of ureter. The ureter's epithelium is visible as a highly folded, stellate-shaped tissue lining the inner surface, consisting of a transitional epithelium, with four or five cell layers. The shape of superficial cells depends on the accumulation of urine in the urinary tract, with characteristic dome-shaped (umbrella cells) or flattened cells, with one or two nuclei, covered by rigid urothelial plaques (densification of the apical membrane). The intermediate layer contains pear-shaped cells, and the basal one consists of small stem cells with a single nucleus.

1.28 Glandular exocrine epithelium - tubular glands – pyloric glands



CHAPTER 2 - Connective tissue proper



Connective tissue is a fundamental tissue in the body, essential for providing structural support, binding other tissues together, storing energy, and facilitating the transport of various materials. It plays a vital role in maintaining the integrity of organs and systems. There are two main categories of adult proper connective tissue: loose and dense, added to embryonic connective tissue.

Loose connective tissue is characterized by a gel-like matrix and a variety of cells, such as fibroblasts, macrophages, and mast cells, which provide elasticity and support. This type of tissue is commonly found beneath epithelial tissues and around blood vessels. One important component of loose connective tissue is the lamina propria, a layer of connective tissue that underlies mucous membranes. The lamina propria provides support to the epithelium, contains blood vessels, and houses immune cells, playing a crucial role in the defense against pathogens.

Dense connective tissue, on the other hand, contains tightly packed collagen fibers that offer strength and resistance to stretching forces. It can be further divided into dense regular, with fibers arranged in parallel (as seen in tendons and ligaments), and dense irregular, where fibers are arranged in multiple directions (found in the dermis of the skin).

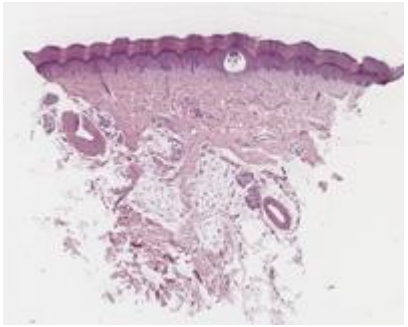
The cells within connective tissue include fibroblasts, which produce fibers and ground substance, and macrophages, which play a role in immune response through phagocytosis. Mast cells are involved in inflammatory responses by releasing histamine, while adipocytes are specialized for fat storage. The extracellular matrix (ECM) of the connective tissue comprises fibers, such as collagen for strength and elastin for elasticity, embedded in a gel-like ground substance that contains proteoglycans and glycoproteins. This matrix fills the spaces between cells and fibers, facilitating nutrient exchange and maintaining tissue hydration.

Embryonic connective tissue is composed of a sparse population of fibroblasts embedded in a thick matrix, rich in collagen fibers. This structure provides both cushioning and support to the umbilical vessels. Histologically, mucous connective tissue appears as a viscous, jelly-like substance, with fewer cells and more ECM compared to mesenchyme.

Histological examination of connective tissues may be done in different staining techniques, including Hematoxylin and Eosin (H&E) for general tissue structure, Masson's Trichrome to highlight collagen fibers or orcein to highlight elastic fibers, added to immunohistochemistry to detect specific cell types or proteins.

Overall, understanding the histology of connective tissue is crucial for recognition of its diverse roles in health and disease, but also provides insights into developmental processes and potential implications in regenerative medicine and tissue engineering.

2.1 Loose connective tissue - Papillary Dermis – Skin



The slide presents a fragment of so-called "thick skin", based on the epidermis thickness, which is mainly found on the palms of the hands and the soles of the feet. Skin epithelium is a keratinized stratified squamous epithelium that consists of five layers: the stratum germinativum, stratum spinosum, stratum granulosum, stratum lucidum, which is difficult to see, and stratum corneum, from basal to apical location. Subjacent dermis is composed of papillary dermis and reticular (deep) layer. Papillary dermis is composed of loose connective tissue, also called areolar tissue, which is characterized by abundance of ground substance, relatively sparse loosely arranged fibers (collagen type I and III - reticular fibers, and elastic fibers), and abundance of capillaries. The presence of many different resident cells (fibrocytes, fibroblasts, macrophages, mastocytes, and adipocytes) and transient cells (lymphocytes, plasma cells, neutrophils, eosinophils, basophils, and monocytes) may be noticed. Papillary dermis is continued, without a conspicuous boundary, with the reticular dermis, which consists of dense irregular connective tissue, rich in thick collagen type I bundles, less ground substance, fewer cells, and relatively larger blood vessels (arterioles and venules). Hypodermis is the next deeper layer, consisting of numerous adipocytes.

2.2 Loose connective tissue – Endometrium

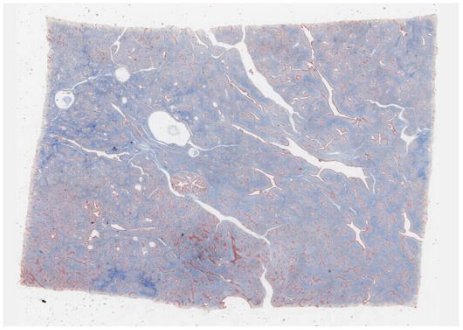
The slide shows a particular type of loose connective tissue located in the inner layer of the uterine wall, named endometrium, composed of lining epithelium, endometrial (uterine) glands, and highly cellular stroma (lamina propria). Endometrium represents a specialized mucosa that undergoes impressive changes during the menstrual cycle. It is composed of two layers: functional layer (stratum functionalis), which represents the upper two thirds of the mucosa that is lost during menstruation and is supplied by spiral arterioles and basal layer (stratum basalis), which forms the lower third of the mucosa that is retained during menstruation and regenerates the functional layer, during each endometrial cycle. During the secretory phase

of the endometrial cycle, depicted in this slide, functional layer is further subdivided into stratum compactum containing decidual (predecidual) cells, active in glycogen secretion, and stratum spongiosum, showing intercellular edema.

2.3 Loose connective tissue - Lamina propria – Jejunum

The slide shows a fragment of jejunum (small intestine), composed of four layers: mucusa, submucosa, muscularis propria (muscularis externa), and serosa. Mucosa consists of simple columnar epithelium with enterocytes and goblet cells, lining intestinal villi and intestinal crypts, lamina propria (loose connective tissue) and muscularis mucosae. Lamina propria contains many cells involved in immune reactions, as it is the primary site where antigens and other foreign substances (e.g. bacteria) may breach the epithelial barrier, stimulating the immune cells. There are also blood and lymphatic vessels, along with smooth muscle fibers extending from the muscularis mucosae to the tip of the intestinal villi.

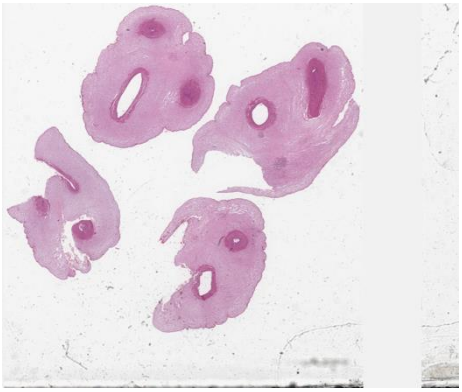
2.4 Dense irregular connective tissue - collagen fibers (Masson's trichrome staining) - Breast



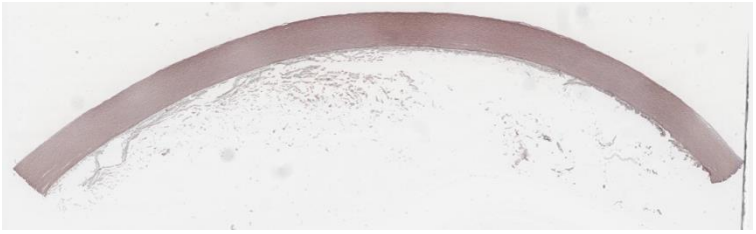
The slide depicts a section of inactive adult mammary gland, to exemplify dense irregular connective tissue. Dense connective tissue is less cellular than loose connective tissue and contains larger and thicker collagen fibers and bundles. Cellular component is formed mainly of fibrocytes and/or fibroblasts. Few blood vessels may be found within this tissue. It may be described as either irregular or regular depending on the arrangement of its fibrous content. Dense irregular connective tissue, depicted in the septa delimitating breast lobules, in this slide, contains collagen fibers, which are randomly interwoven.

2.5 Embryonic connective tissue - Umbilical cord

The slide consists of a section of the umbilical cord, to exemplify embrionic connective tissue. It contains two arteries and a vein surrounded by matrix of mucous embrionic connective tissue (“Wharton’s gelly”) comprised of specialized fibroblast-like cells and mesenchymal cells and occasional mast cells embedded in an amorphous ground substance rich in proteoglycans, mainly hyaluronic acid. Allantoic duct remnant is also visible.

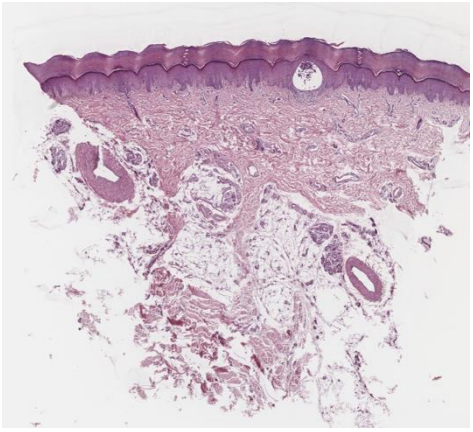


2.6 Elastic fibers - Aorta (orcein staining)



The slides show elastic fibers organized in ellatic lamellae in the media of aorta. Elastic fibers are visible with special staining methods, such as orcein, as depicted in this slide, or resorcin. Elastic lamellae of the elastic arteries are now considered as a product of synthesis of smooth muscle cells rather than fibroblasts. The adventitia is made up of loose connective tissue, containing collagen fibers.

2.7 Dense irregular connective tissue - Deep dermis - Skin

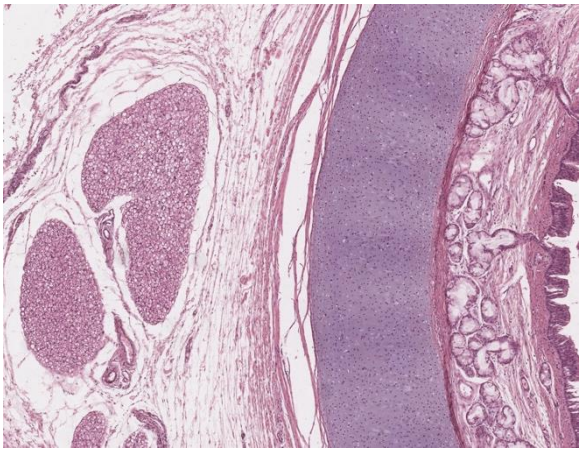


The slide presents a fragment of so-called "thick skin", based on the epidermis thickness, which is mainly found on the palms of the hands and the soles of the feet. Skin epithelium is a keratinized stratified squamous epithelium that consists of five layers. Subjacent dermis is composed of papillary dermis and reticular (deep) layer. Papillary dermis is composed of loose connective tissue and is continued without a conspicuous boundary with reticular dermis, which consists of dense irregular connective tissue, rich in thick collagen type I bundles, less ground substance, less cells, and relatively larger blood vessels (arterioles and venules). Deep dermis cellular component is formed mainly of fibrocytes or/and fibroblasts. Its fibers are randomly interwoven. Other location of dense irregular connective tissue are: periosteum and perichondrium, epineurium, submucosa of the alimentary tract, capsules of liver, lymph nodes, spleen, testes, and other organs. Hypodermis is the next deeper layer, consisting of numerous adipocytes.

2.8 Dense regular connective tissue – Tendon

The slide consists of a longitudinal section of a tendon, which is composed of dense regular connective tissue. Dense connective tissue is less cellular than loose connective tissue and contains larger and thicker fibers. Cellular component is formed mainly of fibrocytes or/and fibroblasts. Few blood vessels may be found within this tissue. Dense regular connective tissue, as that from tendons, is commonly arranged in cords or bands of varying width, composed of tightly packed collagen type I bundles with a parallel and evenly spaced arrangement. Other locations of dense regular connective tissue are: ligaments, aponeuroses, and the stroma of cornea.

CHAPTER 3 - Specialized connective tissue



Specialized connective tissues represent a unique category within the broader connective tissue family, being characterized by specific structural and functional properties that enable distinct roles in the body.

Cartilage, a specialized connective tissue, with firm consistence of its extracellular matrix (ECM), is classified into three types, according to its dominant fiber types, as following: hyaline cartilage, elastic cartilage, and fibrocartilage.

Hyaline cartilage has a smooth, glassy appearance and is found in areas like the nose, the trachea and bronchi, and the ends of long bones.

Elastic cartilage contains numerous elastic fibers, making it flexible, and is located in the ear and epiglottis.

Fibrocartilage, on the other hand, is dense with collagen fibers, providing tensile strength, and is found in intervertebral discs and the pubic symphysis.

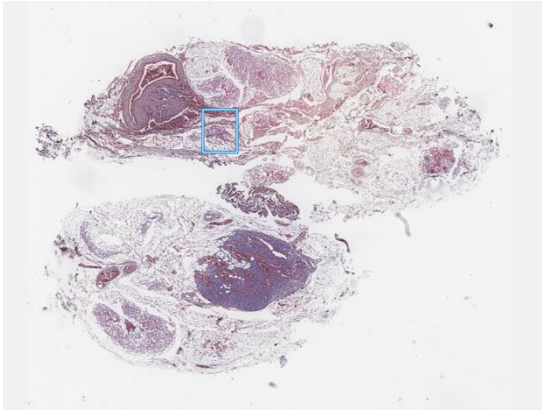
Bone tissue is also a specialized type of connective tissue, with a calcified ECM, and includes compact and spongy (cancellous) types; compact bone is dense and forms the outer layer of bones and most of the structure of diaphysis of long bones, while spongy bone features a lighter, trabecular structure, being found within short and central part of flat bones; spongy bone may be also involved in hematopoiesis.

Adipose tissue consists of two main types: white (unilocular) and brown (multilocular) adipose tissue, although other types of adipose tissue have been identified in recent years.

White adipose tissue stores energy and insulates the body, being characterized by large, lipid-filled cells, disposed in a single inclusion pushing the nucleus to the periphery.

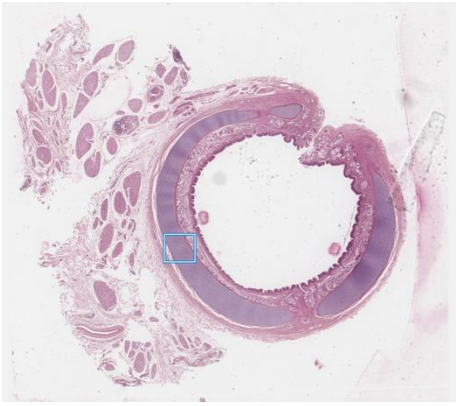
Brown adipose tissue contains cells filled up with multiple lipid droplets and abundant mitochondria, with a central or peripheral rounded nucleus, playing a key role in thermogenesis.

3.1 Brown adipose tissue



The slide contains lobules of brown adipose tissue associated with lobules of white adipose tissue and a fragment of a lymph node. The richly vascularized brown adipose tissue is predominantly composed of multilocular (brown) adipocytes and abundant capillaries. In contrast with white (unilocular) adipocytes, brown adipocytes contain many small lipid droplets and abundant mitochondria, which give the tissue eosinophilic and "spongy" appearance in the hematoxylin & eosin (H&E) staining. The nuclei of brown adipocytes are large, active, and usually with a central location. White adipocytes can often be found in the brown fat pads. Brown adipose tissue is abundant in infants but scant in adults, such as brown adipose depots in supraclavicular, paravertebral, mediastinal, para-aortic, and suprarenal regions.

3.2 Hyaline cartilage – Trachea

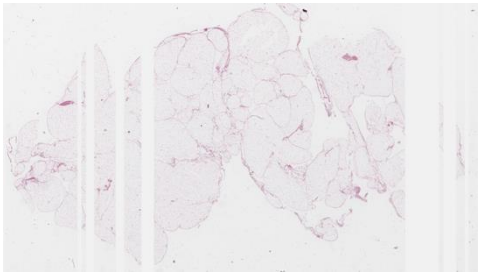


The slide shows a section of trachea, containing C-shaped hyaline cartilage pieces. Hyaline cartilage serves supporting and protective roles. The abundant extracellular matrix appears homogeneous and lacks visible fibers, vessels or nerves. The rounded cartilage cells, chondrocytes, are located in lacunae. The territorial matrix immediately surrounding the lacunae contains mostly proteoglycans and may therefore be more basophilic than the interterritorial matrix rich in collagen type II. The cartilage is surrounded by perichondrium, a sheath of dense connective tissue harboring blood vessels and a small nervous components. Because cartilage progenitor cells reside within the perichondrium, the periphery of cartilage presents small elliptic chondrocytes, while they become round deeper in the cartilage and may form isogenous groups of up to eight cells.

3.3 Elastic cartilage (Orcein staining)

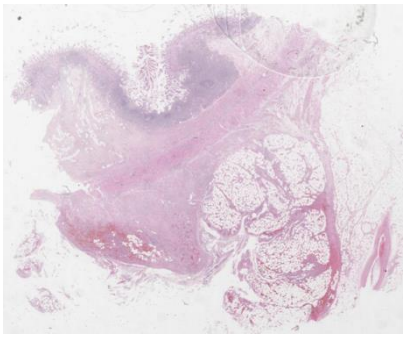
The slide shows an ear lobe containing a central elastic cartilage, covered by skin. The elastic cartilage is composed of rounded chondrocytes and extracellular matrix with abundant elastic fibers, visible as an extensive network in the orcein stain. The avascular elastic cartilage is nourished by diffusion from blood vessels located in the perichondrium surrounding the whole tissue. Because the perichondrium houses the progenitor cells, smaller, elliptical young chondrocytes can be seen at the periphery of cartilage, while the older chondrocytes are larger and round or form rounded isogenous groups, deeper in the cartilage.

3.4 Adipose tissue - Mesenter



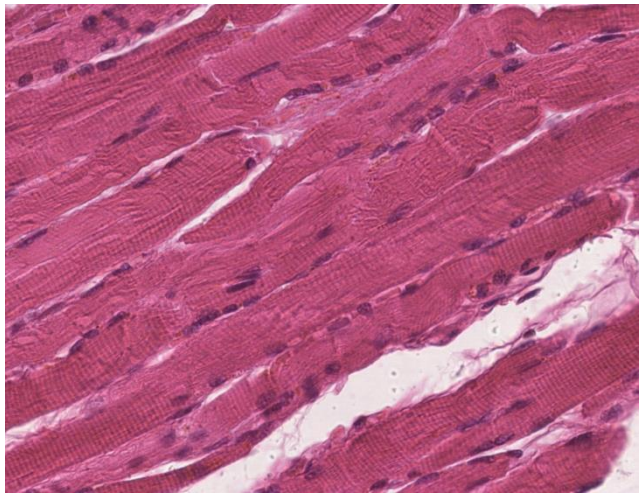
The slide contains a fragment of mesenter, containing white adipose tissue, and lined by peritoneum (connective tissue and mesothelium). White adipose tissue serves as energy storage, as triglycerides, provides thermal insulation, cushions organs, and secretes adipokines. The adipose tissue is predominantly composed of unilocular (white) adipocytes – polyhedral, very large cells that form large aggregates (lobules) or small groups within connective tissue proper. The adipocyte morphology is compared to a signet-ring, as it contains a huge lipid vacuole and a rim of cytoplasm with a small peripheral nucleus. The tissue has a rich network of microvasculature. After dissolution of the lipid vacuole during slide preparation, the cells are rather fragile and may shrink, collapse, or rupture, distorting the tissue architecture.

3.5 Adipose tissue – Ileum



The slide shows a fragment of ileum, containing abundant white adipose tissue. Adipose tissue is composed of fat cells, called adipocytes, connective tissue, and blood vessels. There are two types of adipose tissue, unilocular (white) and multilocular (brown). In this slide we can see the unilocular one. Adipocytes appear empty due to tissue processing that dissolves fatty material. Unilocular adipose cells store triglycerides in a single, large fat droplet, which is not membrane-bounded, and occupies most of the cell. The cytoplasm, nucleus and organelles are located in the peripheral zone. Adipocytes are organised in groups subdivided into lobules by thin connective tissue with a rich vascular supply. Adipose tissue acts also as an endocrine organ because of its secretory function.

CHAPTER 4 - Muscular Tissue



The muscular system is composed of specialized tissues that enable movement and force generation through contraction. From a histological perspective, muscles are classified into three distinct types, based on their structure and function: skeletal, cardiac, and smooth. Each type is made up of elongated cells, known as muscle fibers, that contain actin and myosin filaments, which interact to produce contraction.

Skeletal muscle, which is voluntary, consists of long, multinucleated fibers, with a characteristic striated appearance due to a specific arrangement of sarcomeres - the functional units of muscle contraction. These muscles are attached to bones *via* tendons and play a key role in movement and posture. Histologically, skeletal muscle fibers are surrounded by connective tissue layers: the endomysium, perimysium, and epimysium, from internal to external part, providing the structural support and transmitting the contractile forces.

Cardiac muscle, found exclusively in the heart, also exhibits striations but differs from skeletal muscle in that its fibers are branched and connected by intercalated discs. These specialized junctions contain gap junctions and desmosomes, facilitating synchronized contractions essential for blood pumping. Cardiac muscle cells are typically uninucleated and contract involuntarily.

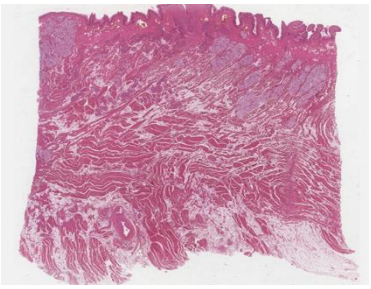
In contrast, smooth muscle lacks striations due to a more random arrangement of its contractile filaments. It is found in the walls of hollow organs, such as the intestines, blood vessels, and the urinary bladder. Smooth muscle cells are spindle-shaped, uninucleated, and contract involuntarily, playing a key role in regulation of the internal processes, such as digestion, blood flow, and airway constriction.

At the cellular level, all muscle types rely on complex biochemical processes involving calcium ions and ATP to initiate contraction.

This chapter will delve into the histological characteristics of each muscle type, highlighting the organization of fibers, the connective tissue's role, and their vascularization and innervation.

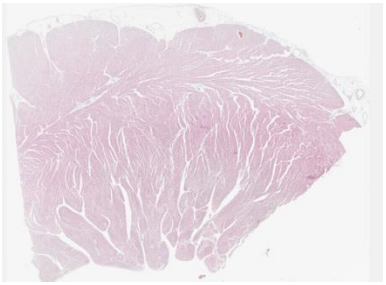
The knowledge of the microscopic features of each type of muscular tissue is essential for understanding how the muscular system supports movement and maintains essential physiological functions.

4.1 Striated skeletal muscle – Tongue



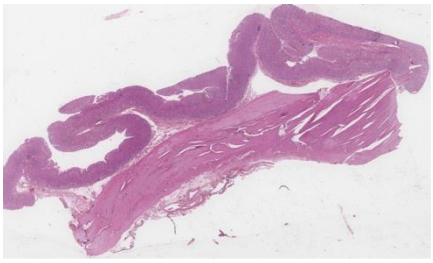
The slide depicts the striated skeletal muscle of the tongue, which is composed of longitudinally and cross sectioned muscle fibers (myocytes) demonstrating striations produced by alternating A-bands (dark) and I-bands (light). The sarcomere is the main contractile unit of the muscle fiber in the skeletal muscle. The structure of the sarcomere is traditionally described with dark and light bands visible under the microscope. This banding pattern in sarcomeres is mainly due to the arrangement of thick and thin myofilaments in each unit. The myocytes are multinucleated with peripherally placed flattened nuclei of subplasmalemmal position (under the plasma membrane). The striated skeletal muscle tissue is voluntary and highly blood supplied.

4.2 Striated cardiac muscle



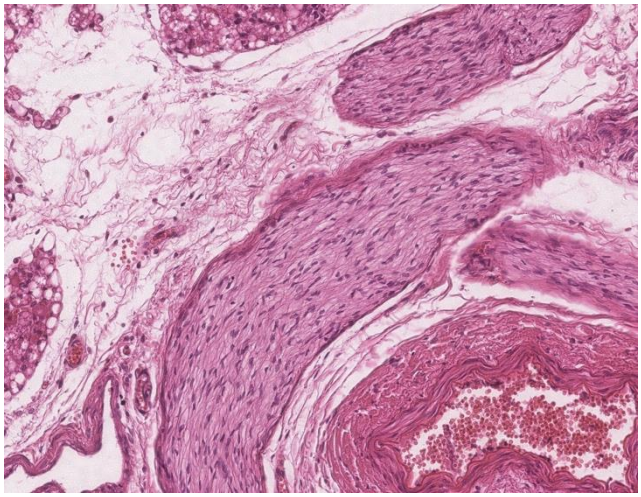
The slide shows a heart section, containing striated cardiac muscle (myocardium), which is composed of branching cardiac muscle cells (cardiac myocytes or cardiomyocytes) with single centrally placed nucleus for each muscle cell. Each of the cell endings is connected with the ending of an adjacent cardiac myocyte via specialized junctions called intercalated disks. They are usually unstained, but occasionally appear as thin, dark lines between adjacent cells. Yellow-brown granules of lipofuscin pigment are visualized near the nucleus of some cells.

4.3 Smooth muscle - Stomach



The slide depicts a section of stomach, containing smooth muscle (muscularis layer), which is a type of involuntary non-striated muscle tissue found in the walls of hollow organs. It is composed of spindle-shaped fibers, grouped in branching bundles. The smooth muscle cells have eosinophilic cytoplasm, which mainly consists of myofilaments. The nuclei of the smooth muscle cells are elongated and centrally placed, taking a cigar-like shape during contraction. There are no visible striations in the cytoplasm of the smooth muscles cells.

CHAPTER 5 - Nervous tissue



The nervous tissue is considered the most complex tissue in the human body. It is formed by a network of billions of neurons, assisted by numerous supporting cells, called glial cells. By collection, analyse, and integration of information from other organs and the external environment, the nervous system continuously stabilizes the blood pressure, the blood glucose, the hormone levels, and others. The nervous system is organised into: central nervous system (CNS), which comprises the brain and spinal cord, and peripheral nervous system (PNS), represented by cranial, spinal, and peripheral nerves, which conduct impulses to and from the CNS (sensory and motor nerves), and ganglia, small groups of neurons and glial cells outside CNS.

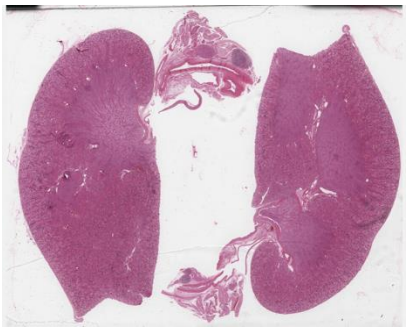
The Autonomic Nervous System (ANS) is the portion of PNS that conducts involuntary impulses to muscles and glandular epithelium. ANS is classified into sympathetic, parasympathetic, and enteric divisions. ANS and its neurons are also named visceral type. While the presynaptic neurons of the sympathetic division are located in the upper lumbar and thoracic regions of the spinal cord, the presynaptic neurons of the parasympathetic division are located in the sacral spinal cord and in the brain stem.

The presynaptic neurons send axons from the upper lumbar and thoracic spinal cord to the paravertebral and vertebral ganglia. The cell bodies of the postsynaptic effector neurons of the sympathetic division are contained within the paravertebral ganglia of the sympathetic trunk.

The presynaptic parasympathetic neurons send axons from the brain stem (midbrain, pons, and medulla), and S2-S4 sacral segments of the spinal cord to visceral ganglia. The cell bodies of the postsynaptic effector neurons of the parasympathetic division are contained within the visceral motor ganglia of cranial nerves X, IX, VII, and III, and within the ganglia in or near the wall of pelvic and abdominal organs.

A peripheral nerve is a bundle of nerve fibers held together by connective tissue. The nerves of PNS are made up of many nerve fibers that transport motor (effector) and sensory information between the body tissues and organs and the spinal cord and brain.
The peripheral nerves consist of nerve fibers and their supporting Schwann cells, fibroblasts and dispersed macrophages and mast cells. The individual nerve fibers and their associated Schwann cells are supported by connective tissue organized into three distinctive components, as following: the endoneurium, which surrounds each individual nerve fiber, consisting of loose connective tissue, the perineurium, which surrounds each nerve fascicle, as a specialized connective tissue that contributes to the formation of the blood-nerve barrier, and the epineurium, the outermost tissue of the peripheral nerve, composed of dense irregular connective tissue that surrounds a peripheral nerve and fills the spaces between nerve fascicles. Adipose tissue is often associated with the epineurium in larger nerves. The blood vessels that supply the nerves travel in the epineurium, and their branches penetrate into the nerve and travel within the perineurium.
In conclusion, this chapter illustrates the histological features of the nervous tissue as a preliminary step in understanding the histology and histopathology of the CNS.

5.1 Autonomic sympathetic ganglia

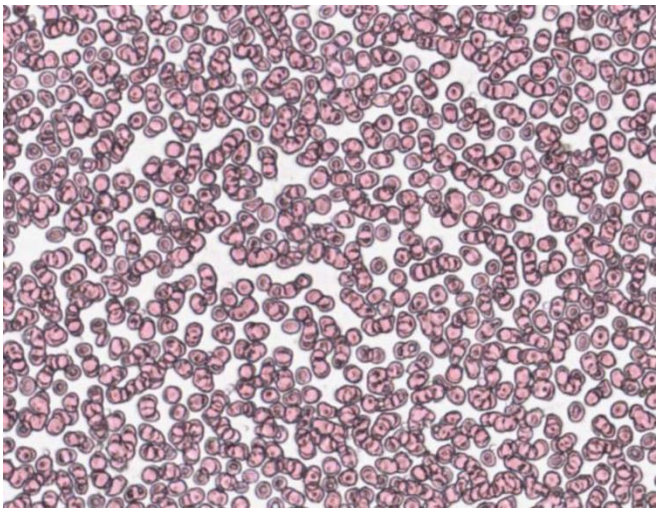


The slide shows autonomic sympathetic ganglia, located in the kidneys vicinity, associated with neurovascular bundles, white and brown adipose tissue, and small-sized lymph nodes. The autonomic sympathetic ganglia have multipolar neurons, which may appear star-shaped in histological sections. The neurons of autonomic ganglia are frequently enveloped by a layer of satellite cells, which is usually incomplete. Different from sympathetic ganglia, only a few satellite cells are seen aorund each neuron in intramural parasympathetic ganglia (located within certain organs, especially in the walls of the digestive tract). There are bundles of nerve fibres visible among the cell bodies of the neurons, which are mainly the axons of the ganglion nerve cells.

5.2 Peripheral nerve - cross section

The slide contains a peripheral nerve visible in cross section. It is covered by epineurium, a layer of collagenous tissue that bundles several nerve fascicles, each containing many nerve fibers. The individual nerve fascicles are contained within a condensed layer of collagenous tissue called the perineurium. Blood vessels run longitudinally within compartments formed by epineurium and perineurium. Within a bundle, nerve fibers and their ensheathing Schwann cells are surrounded by endoneurium, a delicate layer of connective tissue with a capillary network, separated from Schwann cell by a basement membrane.

CHAPTER 6 - Blood & hematopoiesis



Blood is fluid, composed of plasma and cells (red blood cells – RBCs, platelets, and white blood cells – WBCs), formed in bone marrow by a process named hematopoiesis.

RBCs (erythrocytes) are the most common type of blood cell. They have a biconcave disk shape, with a diameter of 6–8 µm and a thickness of 2 µm, being much smaller than most other human cells. The proteins of the membrane skeleton are responsible for their deformability, flexibility and durability, enabling them to squeeze through capillaries, to less than half of their diameter and to recover their shape as soon as the compressive forces cease. Mature RBCs lack nucleus and most organelles. They develop in the bone marrow and circulate for about 100–120 days in the body. These cells' cytoplasm is rich in hemoglobin, an iron-containing molecule that can bind oxygen and is responsible for the blood's red colour.

Platelets or thrombocytes are small, regularly-shaped biconcave disks, of 2- 3 µm diameter, without nuclei, which are derived from fragmentation of precursor cells, named megakaryocytes. The average lifespan of a platelet is normally just 5 to 9 days.

Neutrophils are the most abundant type of WBCs in mammals and form an essential part of the innate immune system. Normally neutrophils contain a nucleus divided into 2-5 lobes. The cytoplasm contains numerous specific neutral granules, added to azurophilic granules.

Eosinophils represent 1-5% of WBCs, being responsible for the fight against parasites. They exhibit a brick-red staining with eosin, in Romanowsky method, concentrated in small granules, which contain chemical mediators, such as histaminase and proteins, eosinophil peroxidase, ribonuclease, deoxyribonucleases, lipase, plasminogen, and major basic protein.

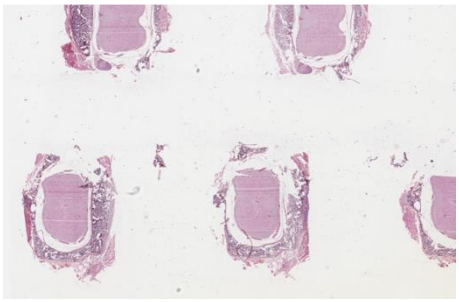
Basophils represent about 0.01% to 0.3% of circulating WBCs. They contain large cytoplasmic granules which obscure the cell nucleus. The nucleus usually has two lobes.

Lymphocytes can be divided into large granular lymphocytes and small lymphocytes. Microscopically, a lymphocyte has a large, dark-staining nucleus with scarce cytoplasm. The dense nucleus of lymphocyte is approximately the size of a red blood cell (about 7 µm diameter).
Monocytes are usually identified in smears by their large kidney shaped or notched nucleus. The cytoplasm stains greyish-blue and contains small azurophilic granules. Monocytes circulate in the bloodstream for about one to three days and then typically move into different tissues. They constitute between 4-8% of the WBCs. They differentiate into tissue resident macrophages or dendritic cells and are responsible for protection against foreign substances.
The human body produces an astonishing 100 billion blood cells each day. This is necessary because blood cells have short lifespan. Hematopoiesis (hemopoiesis) occurs in adults in the bone marrow - the central cavity of the bones. Hematopoiesis starts with hematopoietic stem cells (HSCs), proliferative and multipotent cells that are located in specialized bone marrow regions, called 'niches'. HSCs can become any type of blood cell, a process that is regulated by growth factors and hemopoietic cytokines. Through a series of steps that increase their commitment to become a specific cell type, HSCs ultimately give rise to all RBCs, platelets, and WBCs, which are released into the blood stream.

6.1 Blood smear - May-Grunwald Giemsa staining

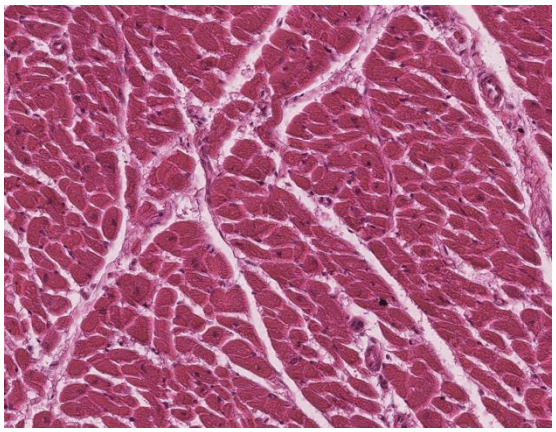
The slide exhibits a blood smear showing red blood cells (erythrocytes), platelets (thrombocytes), and white blood cells (leukocytes). Red blood cells are the most abundant type of blood cell (98%), of reduced size (7-8 µm diameter), anucleate, with a biconcave disc shape, and eosinophilic cytoplasm (bright pink) because of the high concentration of the hemoglobin protein. Platelets are small, basophilic biconcave discs (2-4 µm diameter), aggregated in small groups. White blood cells are classified into granulocytes and agranulocytes. Granulocytes are: neutrophils (polymorphonuclear leukocytes, PMN), with distinctive nuclei exhibiting 2-5 lobes (polymorphic) and azure cytoplasmic granules, eosinophils, with bilobed nucleus, distinctive large, and eosinophilic cytoplasmic granules, and basophils, rare cells with distinctive large, basophilic cytoplasmic granules. Agranulocytes are: lymphocytes and monocytes. Lymphocytes have a size range between 6 and 15 µm diameter and display round nuclei, containing mainly heterochromatin, added to euchromatin in larger ones, and a variable rim of cytoplasm, according to their size corresponding to the degree of maturation. Monocytes are large cells (12-20 µm diameter), with "kidney-shaped" or notched nuclei, with "raked" chromatin appearance, and bluish-gray "ground-glass" cytoplasm.

6.2 Red bone marrow



The slide exhibits a section of a vertebrae surrounding the spinal cord and suprajacent striated muscle. The bone tissue contains red bone marrow. Red bone marrow is the site for the formation of all types of blood cells (hematopoiesis). Its color is given by the hemoglobin in red blood cells (erythrocytes) and it is comprised of hematopoietic cells in various stages of development, reticular connective tissue stromal tissue, and sinusoidal capillaries. Hematopoietic stem cells give rise to red blood cells (erythrocytes), platelets (thrombocytes), and white blood cells (leukocytes). Considering the high cellularity and lack of specific morphology of stem and progenitor cells, the identification of developing blood cells is very difficult, excepting large megakaryocytes (platelets' precursor). These cells are 50 to 70 µm in diameter and exhibit a complex multilobed polyploid nucleus, along with scattered azurophilic granules.

CHAPTER 7 - Cardiovascular system



The cardiovascular system consists of the heart and blood vessels, each characterized by distinct histological structures that are essential for their functions. The heart is composed of three main layers: the epicardium, which serves as the outer layer and is made up of a mesothelial layer along with underlying connective tissue containing blood vessels, nerves, and adipose tissue; the myocardium, which is the thick middle layer, composed of cardiac muscle fibers (myocytes) responsible for contraction; and the endocardium, the innermost layer, lined with endothelial cells, containing connective tissue and specialized conducting cells, known as Purkinje fibers that facilitate electrical impulse transmission.

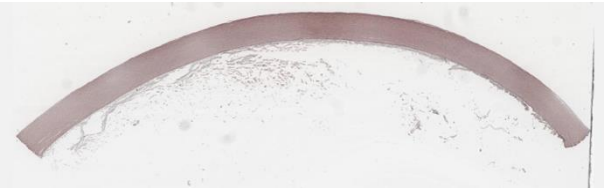
Blood vessels are structured with distinct three layers. In arteries, the innermost layer, or tunica intima, consists of endothelial cells along with a subendothelial layer of connective tissue. The thick middle layer, called the tunica media, is rich in smooth muscle and elastic fibers, involved in the regulation of blood pressure and flow. The outer layer, known as the tunica adventitia, is made up of connective tissue that provides structural support. In contrast, veins typically exhibit thinner walls and larger lumens, often containing valves to prevent backflow; their tunica media is less muscular, while the tunica adventitia is thicker. Capillaries mostly consists of a single layer of endothelial cells, which facilitates the efficient exchange of substances between blood and surrounding tissues and variable associated cells. They can be classified into three types - continuous, fenestrated, and sinusoidal, based on their permeability.

The microscopic aspects of cardiovascular pathology encompass a range of conditions that reveal significant insights into disease mechanisms. Atherosclerosis is characterized by the presence of atherosclerotic plaques in the arterial intima, featuring foamy cells or lipid-laden macrophages and a fibrous cap, made up of smooth muscle cells and collagen, along with a necrotic core filled with lipid debris and inflammatory cells. Myocardial infarction shows distinct stages under microscopic examination, from early changes (0-24 hours), with coagulative necrosis to subacute phase (1-7 days), with macrophage presence and granulation tissue formation, and chronic phase, with fibrotic replacement fibrosis and potential ventricular remodeling.

Myocarditis is characterized by inflammatory infiltration of the myocardium, often with lymphocytes and occasional eosinophils, leading to myocyte necrosis. The histological features can widely vary, depending on the underlying cause, which may include viral infections, autoimmune diseases, or toxic exposures. Pericarditis shows inflammation of the pericardial sac, often with fibrinous exudate and inflammatory cells, leading to a thickened, fibrotic pericardium in chronic cases. Myocardial abscesses result from infections, often revealing necrotic tissue surrounded by neutrophils and granulation tissue, indicating a severe inflammatory response.

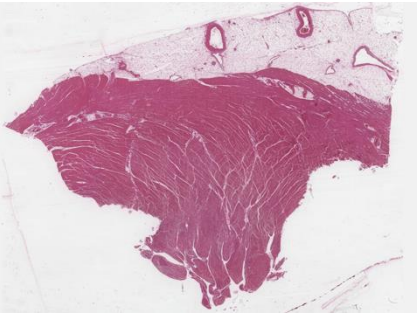
Vascular diseases, such as vasculitis, exhibit inflammatory infiltration and vascular wall damage, while aneurysms are noted for medial degeneration, leading to fibrosis and inflammation.
In summary, the histological structure of the heart and blood vessels is intricately designed to support their functions in circulation and the maintenance of blood pressure. Understanding these components at the microscopic level is crucial for the study of normal cardiovascular system and its diseases.

7.1 Aorta - elastic fibers (orcein) staining



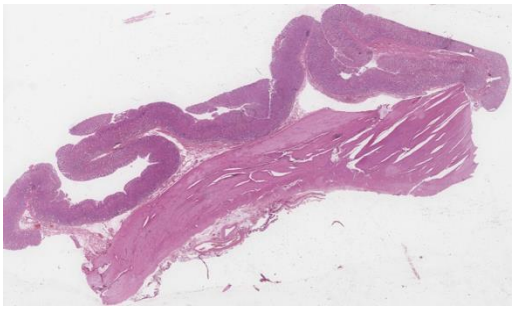
The wall of the aorta consists of three layers. Tunica intima is the most internal layer, lined with endothelium. Tunica media is located in the middle; it is the thickest layer, mainly made of elastic fibers, organized in fenestrated elastic membranes (elastic lamellae). Tunica adventitia is the most external layer, composed of loose connective tissue, capillaries, and nerve endings.

7.2 Heart



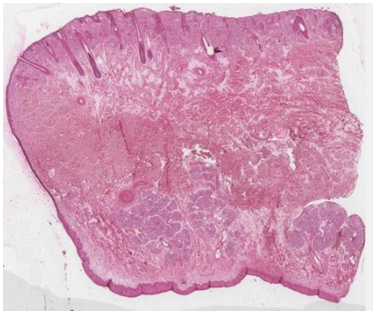
Heart wall is composed of three layers – endocardium, myocardium, and epicardium. Endocardium is the most internal layer, which is made up of a thin layer of endothelium, a middle layer of dense connective tissue and smooth muscle, and a deeper subendocardial layer which contains Purkinje fibres. Myocardium is the middle and the thickest layer of the heart wall, composed of striated cardiac muscle tissue. It consists of cardiomyocytes, connected via intercalated disks and it has a risch blood supply. Epicardium is at the outer surface of the heart, made of a single layer of mesothelial cells (visceral pericardium) and underlying connective and white adipose tissue. Larger blood vessels are found in this layer.

7.3 Arterioles - Stomach fundic region



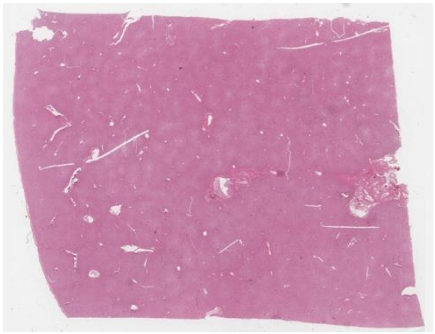
Arterioles are less than 0.5 mm in diameter, with a narrow lumen. The lumen is lined by a single layer of endothelial cells. The subendothelial layer is very thin and an internal elastic lamina is lacking except in the largest arterioles. The tunica media is composed of 1-5 circularly arranged layers of smooth muscle cells. The adventitia is thin and shows no external elastic lamina.

7.4 Continuous capillaries - Lip



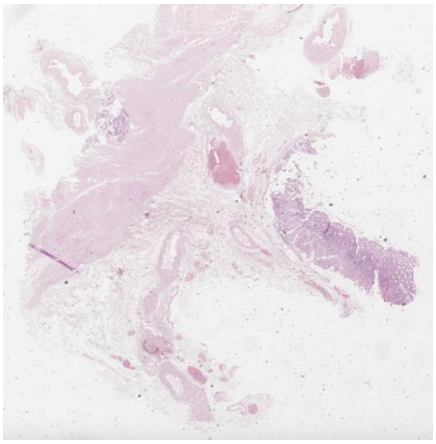
Continuous capillary is characterized by the lack of fenestrae (pores) in its wall. The wall is composed of a single layer of endothelial cells of mesenchymal origin, with polygonal shape and elongated in the direction of blood flow. The endothelial cells rest on a basal lamina, a product of endothelial origin. There are mesenchymal cells with long cytoplasmic processes that partially surround the endothelial cells – pericytes with potential for differentiation into other cells and contractile function. The lumen of the capillaries is filled with red blood cells - erythrocytes.

7.5 Sinusoids - Liver



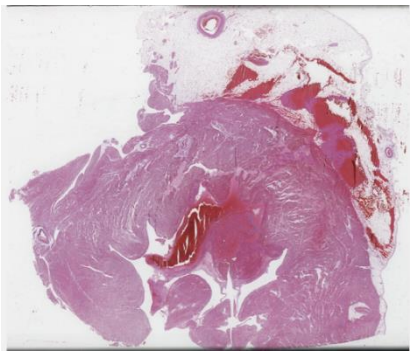
Liver sinusoids are low pressure vascular channels that receive blood from terminal branches of the hepatic artery and portal vein, at the periphery of hepatic lobules, and deliver it to central veins. Sinusoids are lined with endothelial cells and surrounded by plates of hepatocytes. Sinusoids drain into the central veins. The space between sinusoidal endothelium and hepatocytes is called the space of Disse. Sinusoidal endothelial cells are highly fenestrated, which allows flow of plasma from sinusoidal blood into the space of Disse. Another important characteristic of hepatic sinusoids is that they house an important part of the phagocytic system due to the presence of numerous Kupffer cells, a type of fixed macrophages.

7.6 Arterioles and venules – Stomach fundic region



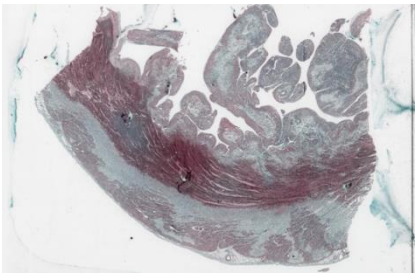
There are three distinct layers forming the walls of arteries and veins. The innermost layer is the tunica intima, lined by endothelium of simple squamous epithelial cells. Deep to the endothelium there is a basement membrane and a layer of subendothelial connective tissue for support of the overlying cells. The middle muscular layer of the arteries and veins is the tunica media, made of smooth muscle tissue. The outermost layer is the tunica adventitia, also known as tunica externa. This layer is primarily composed of type I collagen and elastic connective tissue (in arteries) and is responsible for anchoring the vessels to adjacent organs.
The larger arteries contain two additional layers – the external and internal elastic laminae. The internal elastic lamina is a wavy band of elastic fibers between the intima and media, while the external one is seen between the media and adventitia. Tunica media is significantly thinner in veins when compared to arteries of roughly the same size. Veins have wider lumen, contain valves, and are classified as small, medium, and large veins. The valves prevent the backflow of blood in the low-pressure venous system.

7.7 Acute transmural myocardial infarction



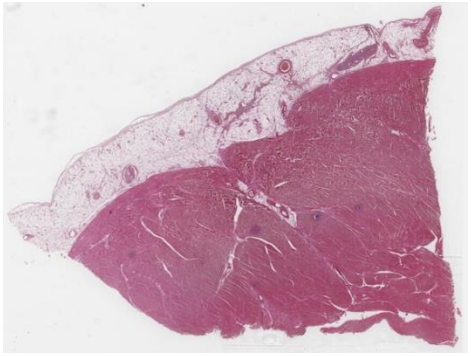
The slide shows areas of myocardium with loss of cross striations, exhibiting contraction bands and edema. There are areas of coagulative necrosis, with nuclei pyknosis, myocardial hemorrhage, and neutrophilic infiltrate. Areas of transmural hemorrhage are also involving epicardium and endocardium and are focally associated with fibrin deposits. There is also a mural thrombus partially adherent to endocardium.

7.8 Myocardial infarction in variable phases



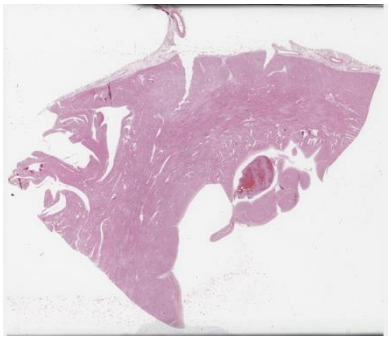
The slide shows cardiomyocytes abnormalities, with cytoplasmic hypereosinophilia and edema, contraction band necrosis, with areas of evident coagulative necrosis associated with hemorrhage and neutrophilic infiltrate (acute phase). There is focal macrophage infiltration, added with fibroblasts (subacute phase). Supplementary, there are areas with cardiomyocytes drop out leading to interstitial fibrosis, hemosiderin laden macrophages, early granulation tissue, and fibroblast proliferation (remote or healing phase).

7.9 Acute myocarditis and pericarditis



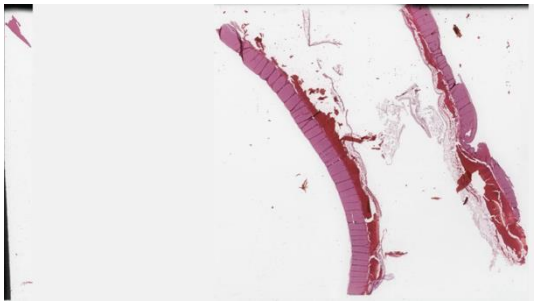
The slide shows the presence of a diffuse myocardium inflammatory infiltrate, associated with myocytes necrosis, and myocardium edema, without the settings of ischemic damage as a consequence of coronary artery atherosclerosis. There are also multiple small myocardium microabscesses. The pericardium has fibrin deposits along with pericardial inflammatory infiltrate.

7.10 Viral myocarditis



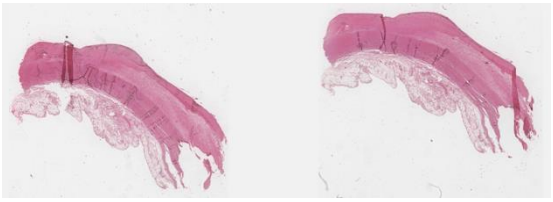
The slide shows, according to Dallas criteria, focal or diffuse mononuclear infiltration of myocardium (lymphocytes and macrophages), with 14 cells / mm2, associated with cardiomyocytes necrosis. Additionally, surrounding myocardial edema may be observed.

7.11 Ruptured aortic aneurysm



The slide shows a large elastic artery with a thinned wall with medial degeneration, loss of smooth muscle cells, and deposition of mucoid extracellular matrix, associated with medial fibrosis. The border between tunica media and tunica intima is obscured. There is a focal inflammatory reaction (lymphocytes and macrophages), along with medial neovascularization. There is also a rupture of the wall, with hemorrhage and fibrin deposits.

7.12 Aortic atherosclerosis

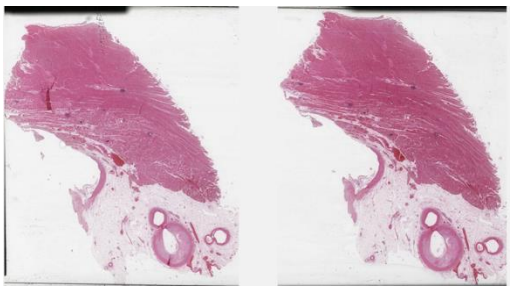


The slide shows a fibrous cap atheroma, composed of neutral lipids, cholesterol crystals, fibrin, covered by smooth muscle cells, histiocytes, lymphocytes, collagen and elastic fibers, and proteoglycans (connective tissue matrix), along with intra-cellular and extra-cellular lipids.

7.13 Coronary atherosclerosis

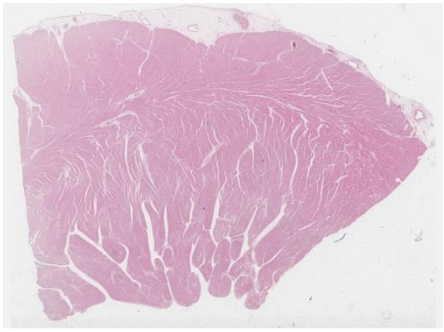
The slide shows a fibrous cap atheroma, with a necrotic core, composed of neutral lipids, cholesterol crystals, foamy macrophages, fibrin, Calcium salts, and fibrous tissue with neoangiogenesis, covered by a fibrous collagenous cap, mixed with smooth muscle cells, histiocytes, lymphocytes, collagen and elastic fibers, and proteoglycans (connective tissue matrix), along with intra-cellular and extra-cellular lipids.

7.14 Myocardial microabscesses



The slide shows multiple small abscesses disposed in myocardium, containing predominantly neutrophils, added to reduced areas of cardiomyocytes necrosis and microorganisms' colonies. There are also intimal coronary fibrous plaques, with a significant luminal diameter reduction. Areas of ischemic myocardial fibrosis are also detected.

7.15 Heart

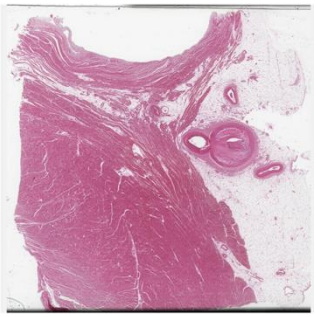


The slide shows the wall of the heart composed of external epicardium, which is lined on the outer surface by mesothelial cells supported by connective tissue, covering loose adipose tissue. The next layer is myocardium, which is the thickest, middle layer of cardiac muscle. Myocardium is rich in blood vessels. Cardiac muscle is striated, involuntary muscle, composed of cardiomyocytes, with single central nuclei, and frequent branches, seen in longitudinal incidences. Specialized junctions between neighboring cardiomyocytes are intercalated discs, which are seen as thin, dark stained linear structures dividing adjacent cells, oblique or perpendicular to the long axis of the cells. There are also yellow-brown perinuclear granules representing lipofuscin pigment, as residual lysosomes. The inner layer is endocardium, which is composed of a simple squamous epithelium supported by a thin layer of connective tissue.

7.16 Aorta - elastic fibers (orcein) staining

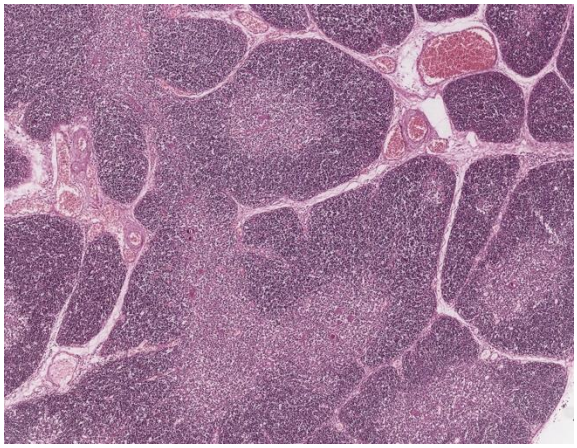
The wall of the aorta consists of three layers. Tunica intima is the most internal layer, lined with endothelium. Tunica media is located in the middle; it is the thickest layer, mainly made of elastic fibers, organized in fenestrated elastic membranes (elastic lamellae). Tunica adventitia is the most external layer, composed of loose connective tissue, capillaries, and nerve endings.

7.17 Coronary artery thrombus



The slide shows a thrombus during organization within a coronary artery. There are associated cardiomyocytes abnormalities, with cytoplasmic hypereosinophilia and edema, contraction bands, added to ischemic myocardial fibrosis.

CHAPTER 8 - Immune System



The immune system is responsible for defense of the body against pathogens and it maintain the overall homeostasis by distinguishing between self and non-self. It comprises a complex network of cells, tissues, and organs that work together to identify and eliminate harmful microorganisms, viruses, and other foreign invaders. The immune system can be divided into two broad categories based on function: innate immunity and adaptive immunity.

From an anatomical and functional perspective, the immune system includes: *innate immunity*, which provides the body's first line of defense and consists of physical barriers (e.g., skin and mucous membranes), cellular components (e.g., neutrophils, macrophages, and dendritic cells), and molecular mediators (e.g., cytokines and complement proteins) and *adaptive immunity* , which involves highly specialized lymphocytes, including B and T cells, and develops memory of previous infections, providing long-lasting and specific protection.

The immune system performs several key functions: recognition of pathogens, neutralization of harmful agents, elimination of infected or abnormal cells, maintenance of immune memory, tissue repair, and regulation of inflammatory responses, preventing the body from damaging its own tissues. The adaptive component of the immune system provides targeted responses through the production of antibodies by B cells and the cytotoxic activity of T cells.
Most of the innate immune system components are distributed in tissues, blood, and lymphatic fluid, allowing rapid detection and response to infections. Cells like macrophages and neutrophils phagocytize pathogens, while dendritic cells act as antigen-presenting cells (APCs), as a link between the innate and adaptive responses. Complement proteins, produced by liver, assist in pathogen destruction by opsonization, lysis, and recruitment of inflammatory cells.

Lymphoid organs are critical for the development and function of immune cells. These include: primary lymphoid organs: the bone marrow (where B cells mature) and the thymus (where T cells

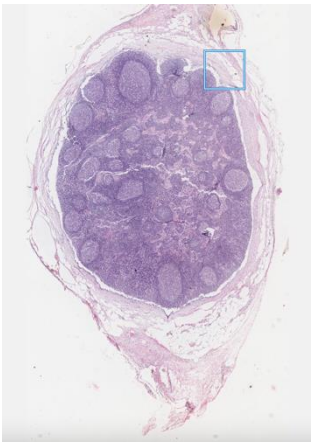
mature) and secondary lymphoid organs: lymph nodes, spleen, and mucosal-associated lymphoid tissue (MALT), which facilitate the interaction between immune cells and antigens.

The immune system's complex regulation involves several signalling pathways that guide cellular activation, proliferation, and differentiation. Cytokines, such as interleukins, interferons, and tumor necrosis factors, play key roles in coordinating immune responses. Immunoglobulins, secreted by plasma cells, neutralize pathogens or mark them for destruction by phagocytes.

The immune system can be affected by various factors, including infections, autoimmune diseases, immunodeficiencies, and cancers. Viral infections can compromise both innate and adaptive immune defenses, leading to increased susceptibility to secondary infections. Autoimmune diseases arise when the immune system mistakenly attacks the body's own tissues, while immunodeficiencies result in a weakened immune response. Lymphoid tissues, such as the lymph nodes and spleen, are common sites for malignancies, including lymphomas and leukemias.

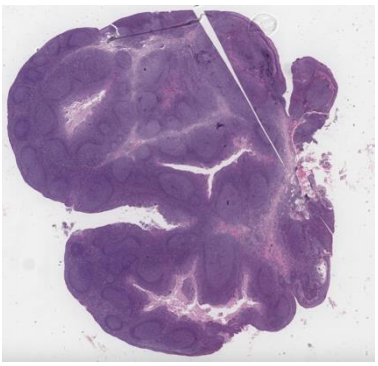
This chapter provides an overview of the histological features of the immune system, a foundational understanding necessary for exploring the pathophysiological changes associated with conditions such as autoimmune diseases, primary immunodeficiencies, hypersensitivity reactions, and malignancies like Hodgkin's lymphoma and non-Hodgkin's lymphoma.

8.1 Lymph node



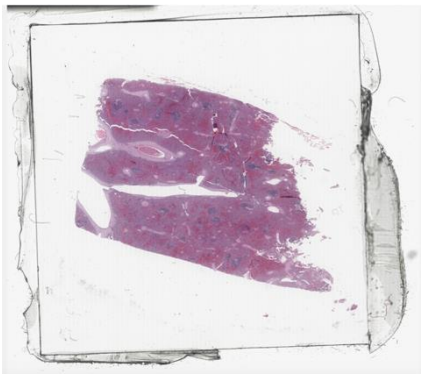
The slide exhibits a lymph node. It has a convex surface where afferent lymphatics enter the organ and a concave depression, the hilum, where an efferent lymphatic leaves and where arteries, veins, and nerves have access to the organ. A dense connective tissue capsule surrounds the lymph node, extending internal trabeculae, through which the blood vessels branch. Lymph node scaffold is formed by reticular tissue, composed of reticular cells and reticular fibers. Beneath the capsule and along trabeculae, lymph flows through vessels forming subcapsular sinus, followed by trabecular sinuses in cortex and medullary sinuses in medulla. Superficial cortex contains lymphatic nodules, mainly composed of B cells and paracortex, mainly occupied by T cells. Medulla is formed by sinuses divided by medullary cords. B cells, macrophages, plasma cells may be found in sinuses. Characteristic high-endothelial venules (HEVs) are located in deep cortex (paracortex), triggering diapedesis of lymphocytes from blood to lymph node.

8.2 Palatine tonsil



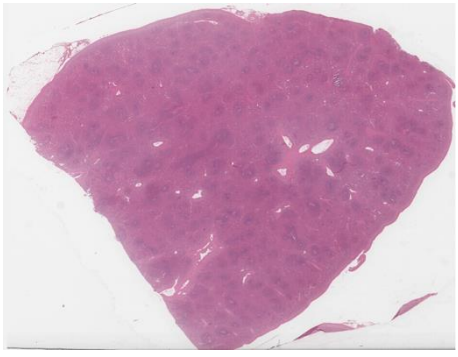
The slide shows one of the components of the mucosa-associated lymphoid tissue (MALT), the palatine tonsil. It is a non-encapsulated organ, situated in the oral lamina propria. It is covered by stratified squamous non-keratinized epithelium, that sends infoldings into the underlying tissue, forming the tonsillar crypts, containing cellular debris along with inflammatory cells. The lymphocytes are distributed as lymphoid follicles, frequently displaying germinal centers and diffuse lymphoid tissue. There is a fibrous hemicapsule at its base.

8.3 Spleen #1



The slide shows the spleen, with a capsule composed of dense irregular connective tissue added with myofibroblasts enclosing the organ. The capsule sends trabeculae that extend inward, containing trabecular blood vessels. The parenchyma is composed of white pulp, comprising lymphatic tissue, organized into periarterial lymphatic sheaths (PALS), as clusters of T lymphocytes around a central arteriole, branch of a trabecular artery, and splenic (Malpighi) nodules, as clusters of B lymphocytes located around central arterioles, depicting a germinal center. The marginal zone is the transition area between white and red pulp where different lymphoid cells interact. Red pulp, disposed between the components of white pulp, contains splenic sinusoids, lined by endothelial cells, along with splenic cords (of Billroth), containing red blood cells, macrophages, lymphocytes, and plasma cells.

8.4 Spleen #2



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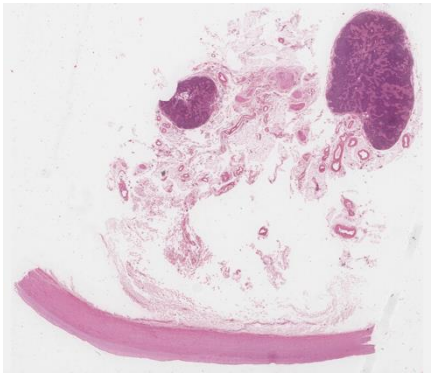
8.5 Lymph node #2



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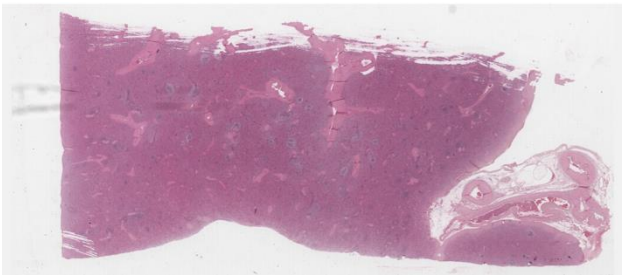
8.6 Spleen #3



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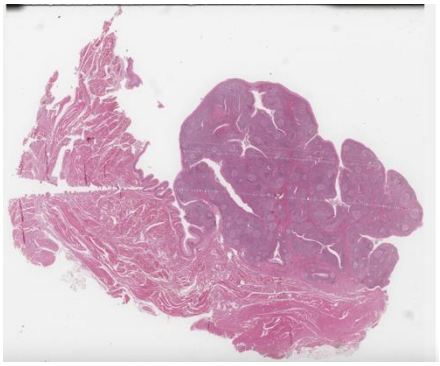
8.7 Thymus

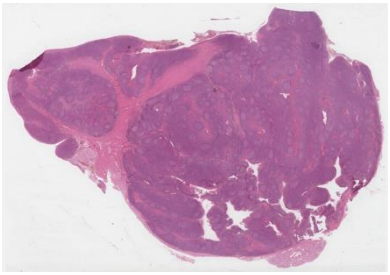
The thymus depicted in this slide has a vascularized connective tissue capsule that extends septa into the parenchyma, dividing the organ into many incompletely separated lobules. Each lobule has an outer darkly basophilic cortex surrounding a more lightly stained medulla. The staining differences reflect the much greater density of lymphoblasts and small lymphocytes in the cortex than in the medulla. The thymic cortex contains an extensive population of T lymphoblasts (or thymocytes), some newly arrived via venules, located among numerous macrophages and associated with the unique three types of thymic epithelial cells (TECs) or epithelioreticular cells that have certain features of both epithelial and reticular cells. These cells usually have large euchromatic nuclei but are morphologically and functionally diverse. There is a blood-thymus barrier, formed by endothelial cells, pericytes and TECs. The paller medulla contains less thymocytes and medullary TECs, of three types. Large aggregates of TECs, sometimes concentrically arranged, called Hassall corpuscles are formed by epithelioreticular cells type VI epithelioreticular cells. Up to 100 µm in diameter, thymic corpuscles are unique to the medulla. They stain with eosin due to presence of keratin intermediate filaments.

8.8 Palatine tonsil #2



Palatine tonsils, located posteriorly to the soft palate, are covered by stratified squamous epithelium. The surface area of each tonsil is enlarged with 10-20 deep invaginations or tonsillar crypts in which the epithelial lining is densely infiltrated with lymphocytes and other leukocytes. The lymphoid tissue is diffusely filled with lymphocytes, with many secondary lymphoid follicles (nodules) around the crypts. This tissue is underlain by dense connective tissue acting as a partial capsule.

8.9 Palatin tonsil #3



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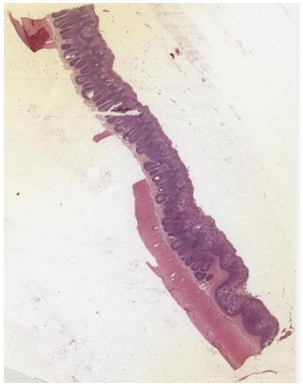
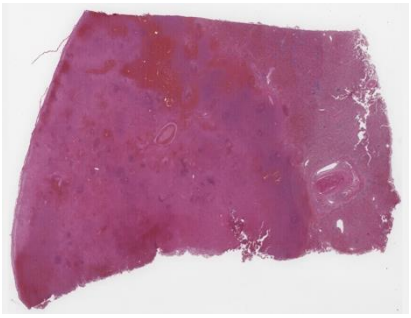


8.10 Peyer patches – Ileum

Peyer's patches are very large clusters of lymphoid follicles located in the wall of the ileum, which allow close monitoring of microorganisms in the gut. No villi cover this portion of small intestine. Highly porous epithelium with special M (microfold) cells are disposed on the apical portion of patches. Numerous plasma cells and other diffuse lymphoid tissue cells may be seen.

8.11 Spleen infarction



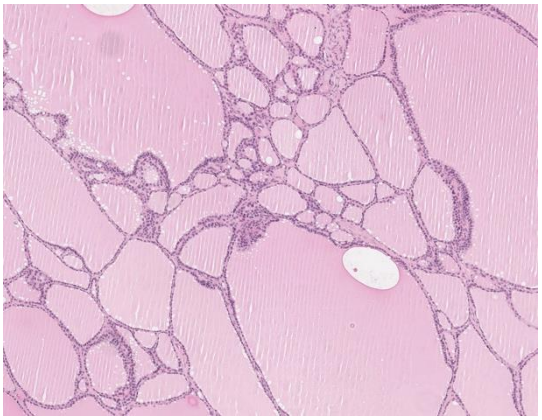
The slide shows a trabecular artery occlusion by an organized thrombus accompanied by other smaller thrombi, corresponding to an early infarction area with different staining pattern compared to the uninvolved parenchyma counterpart. This area shows early necrosis with focal loss of elements of white and red pulp and delimitation by a band of inflammatory cells. Areas of coagulative necrosis contain remnant "ghost" outlines of vessels, lacking cell nuclei. Variable areas of hemorrhage are associated with the recent infarcted area. The superjacent capsular surface is covered by a fibrin deposit.

8.12 Spleen Reticulin fibers

Special stain with silver nitrate shows reticulin fibers forming spleen's scaffold. The parenchyma is composed of white pulp, comprising lymphatic tissue, organized into periarterial lymphatic sheaths (PALS), as clusters of T lymphocytes around a central arteriole, branch of a trabecular artery, and splenic (Malpighi) nodules, as clusters of B lymphocytes located around central arterioles, depicting a germinal center. The marginal zone is the transition area between white and red pulp where different lymphoid cells interact. Red pulp, disposed between the components of white pulp, contains splenic sinusoids, lined by endothelial cells, along with splenic cords (of Billroth), containing red blood cells, macrophages, lymphocytes, and plasma cells. The capsule sends trabeculae that extend inward, containing trabecular blood vessels.

CHAPTER 9 - Endocrine System

The endocrine system is composed of a network of glands that secrete hormones directly into the bloodstream, regulating a wide range of physiological processes. From a histological perspective, this system is characterized by highly vascularized tissues that enable efficient hormone secretion and distribution. Hormones, as chemical messengers, act on target cells and organs, controlling vital functions such as metabolism, growth, reproduction, and homeostasis.



Endocrine glands are composed of specialized epithelial cells arranged in clusters, cords, or follicles, depending on the gland type. The major endocrine glands include the pituitary, thyroid, parathyroid, adrenal, and pineal glands, as well as the pancreas, which has both endocrine and exocrine components. Unlike exocrine glands, endocrine glands release hormones directly into the bloodstream *via* capillary networks that surround the secretory cells.

The pituitary gland (hypophysis) is divided into the anterior and posterior lobes. The anterior lobe, or adenohypophysis, consists of glandular epithelial cells arranged in cords that produce a variety of hormones, such as growth hormone (GH) and adrenocorticotropic hormone (ACTH). In contrast, the posterior lobe, or neurohypophysis, contains axonal projections from hypothalamic neurons, storing and releasing oxytocin and vasopressin.

The thyroid gland is notable for its follicular structure, with spherical follicles lined by simple cuboidal epithelium that produce thyroid hormones (T3 and T4). These follicles are filled with colloid, a glycoprotein-rich substance, as a hormone precursor. Parafollicular cells (C cells), located between the follicles, secrete calcitonin, which regulates calcium homeostasis.

The adrenal glands consist of two distinct regions: the cortex and the medulla. The cortex, derived from mesodermal tissue, is divided into three zones (zona glomerulosa, zona fasciculata, and zona reticularis) that produce steroid hormones, such as aldosterone, cortisol, and androgens. The medulla, derived from neural crest cells, contains chromaffin cells that secrete catecholamines (epinephrine and norepinephrine), in response to stress.

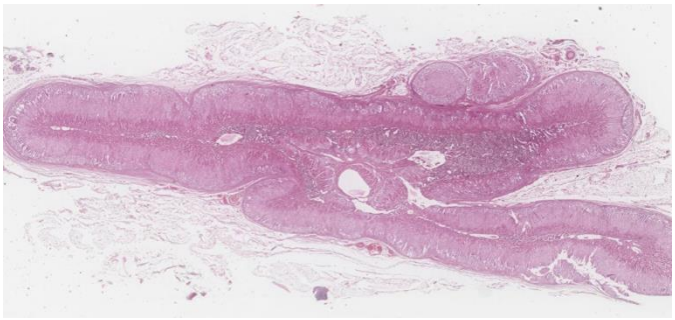
The endocrine pancreas, an essential component of the endocrine system, is composed of clusters of specialized cells, islets of Langerhans that contain alpha cells (secrete glucagon), beta

cells (produce insulin), and delta cells (release somatostatin). The close interaction between insulin and glucagon maintains glucose homeostasis. Histologically, the islets are interspersed among the exocrine pancreas and are richly supplied with blood vessels.

Each endocrine gland has a unique histological architecture tailored to its specific functions, but all share a common reliance on rich capillary networks. This chapter will explore the detailed histology of the endocrine glands, focusing on cellular organization and hormone production and release, as an essential knowledge required to understand their role in maintaining physiological balance and responding to environmental changes.

The endocrine system can be affected by a range of pathologies that disrupt hormone production or action. Common disorders include hyperthyroidism and hypothyroidism, caused by excess or deficient thyroid hormone production, respectively, often due to autoimmune conditions like Graves' disease or Hashimoto's thyroiditis. Diabetes mellitus, a disorder of insulin production or sensitivity by the pancreas is a leading cause of morbidity worldwide. Adrenal disorders, such as Cushing's syndrome and Addison's disease, arise from imbalances in cortisol production, while pituitary adenomas can result in abnormal secretion of multiple hormones, leading to conditions like acromegaly or hypopituitarism.

9.1 Adrenal gland



The slide shows the adrenal gland. The paired adrenal glands are located at the superior pole of each kidney. They are enveloped by a dense connective tissue capsule that sends thin trabeculae into the gland’s parenchyma. The stroma is composed of reticular fibers supporting the secretory cells and microvasculature. Each adrenal gland consists of outer, well vascularized cortex and pale staining, inner medulla with prominent central vein. The cells of adrenal cortex secrete steroid hormones and they are arranged into three layers:

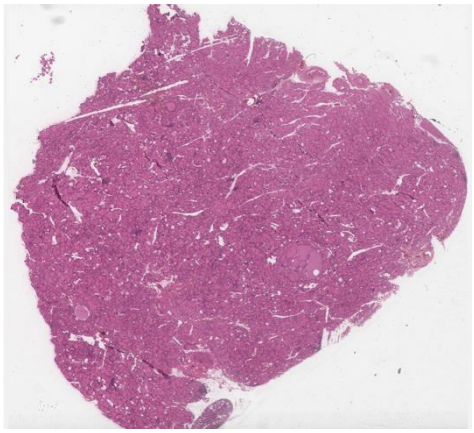
a. Zona glomerulosa – located immediately beneath the capsule and comprising about 15% of the cortex; it contains rounded clusters of columnar or pyramidal cells secreting mineralocorticoids (especially aldosterone).

b. Zona fasciculata – a middle layer that occupies 65-80% of adrenal cortex; it is made up by long cords of large, polyhedral cells filled with lipid droplets. They secrete glucocorticoids (principally cortisol).

c. Zona reticularis – the innermost layer that comprises about 10% of adrenal cortex; it consists of small, well-stained cells arranged in irregular cords interspersed with wide capillaries. The cells secrete primarily weak androgens, including dehydroepiandrosterone (DHEA).

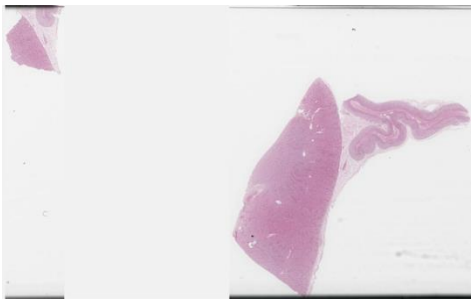
The adrenal medulla is composed of large, pale-staining, polyhedral parenchymal (chromaffin) cells, which resemble sympathetic neurons. These cells are arranged in cords or clumps and supported by a reticular fibers and sinusoidal capillaries. Chromafin cells secrete catecholamine hormones (epinephrine and norepinephrine).

9.2 Thyroid and parathyroid glands



The slide shows the thyroid gland, enveloped by a capsule of fibro-elastic connective tissue, which gives rise to fine collagenous septa breaking gland into lobules. The parenchyma of the thyroid contains rounded thyroid follicles of variable diameter, lined by simple epithelium of thyrocytes (follicular cells) and central lumen densely filled with gelatinous acidophilic colloid composed of thyroglobulin. Thyroid stroma is well vascularized with fenestrated capillaries. The shape of thyrocytes (follicular cells) varies from squamous to low columnar. Thyrocytes rest on a basal lamina and exhibit round and centrally located nuclei, abundant rough endoplasmic reticulum (rER), Golgi complexes, secretory granules, numerous phagosomes, lysosomes, and microvilli. They secrete thyroid hormones – T3 and T4. The parafollicular cells (C cells) may be found inside the basal lamina of the follicular epithelium or as isolated clusters between follicles. They are usually larger than follicular cells and stain less intensely. Numerous, small secretory granules of C cells contain calcitonin. There is also a fragment of a parathyroid gland embedded in the fibrous capsule of thyroid gland; delicate septa divide the gland into dense, cord-like masses of secretory cells. These cells, called principal (chief) cells, are small polygonal, with round, prominent nuclei and pale-staining, slightly acidophilic cytoplasm, containing parathyroid hormone (PTH) granules. Much smaller populations of oxyphil cells, larger than principal cells, with strong eosinophilic cytoplasm, often clustered, are probably inactive, degenerated derivatives of chief cells.

9.3 Adrenal gland and ipsilateral kidney



The slide shows the adrenal gland located at the superior pole of the ipsilateral kidney. They are enveloped by a dense connective tissue capsule that sends thin trabeculae into the gland's parenchyma. The stroma is composed of reticular fibers supporting the secretory cells and microvasculature. Each adrenal gland consists of outer, well vascularized cortex and pale staining, inner medulla with prominent central vein. The cells of adrenal cortex secrete steroid hormones and they are arranged into three layers:

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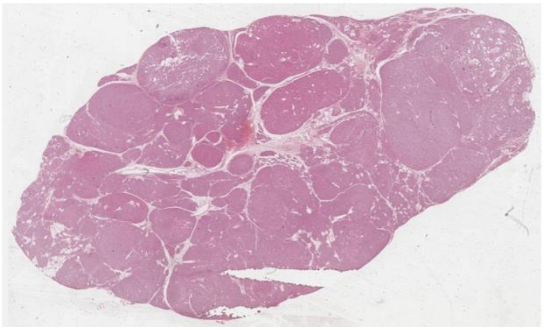
9.4 Pituitary gland #1

The slide contains the pituitary gland, which is composed of an anterior part (adenohypophysis) and a posterior part (neurohypophysis) that is directly attached to the hypothalamus region of the brain by an infundibular stalk. The adenohypophysis consists of a large pars distalis (anterior lobe), mainly seen in this section, the pars tuberalis (cranial part) and thin pars intermedia adjacent to the pars nervosa. The neurohypophysis contains large pars nervosa and infundibulum stalk that is attached to the hypothalamus at the median eminence. Pars distalis consists of cords of cells with different staining affinities (chromophils and chromophobes) surrounded by fenestrated capillaries and supporting reticular connective tissue. Chromophils include basophils and acidophils, named for their affinities for basic and acidic dyes, respectively. The chromophobes are virtually unstained. Pars intermedia is a narrow zone laying between the pars distalis and the pars nervosa; contains basophils, chromophobes, and colloid-filled cysts of various sizes derived from the lumen of the embryonic hypophyseal pouch. Pars nervosa is composed of elongated glial cells known as

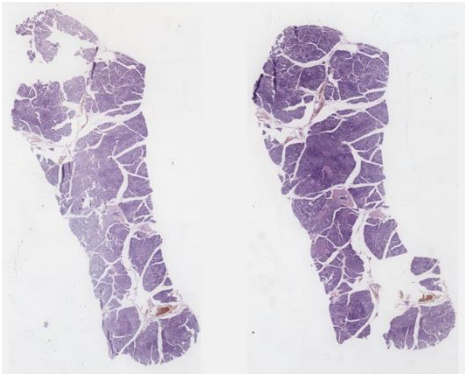
pituicytes. These cells appear to support numerous unmyelinated nerve fibers traveling from the hypothalamus via the hypothalamo-hypophyseal tract. Neurosecretory materials pass along these nerve fibers and are stored in expanded regions at the termination of the fibers, which are referred to as Herring bodies. Pars nervosa also contains a rich network of blood vessels, mainly fenestrated capillaries.

9.5 Parathyroid



The slide shows a section of a parathyroid gland. Each parathyroid gland is usually embedded in the fibrous capsule of thyroid gland; delicate septa divide gland into dense, cord-like masses of secretory cells. The connective tissue stroma is associated with variable amount of white adipose cells. The endocrine cells of the parathyroid glands, called principal (chief) cells, are small polygonal cells with round, prominent nuclei and pale-staining, slightly acidophilic cytoplasm. Their cytoplasmic secretory granules contain the parathyroid hormone (PTH), an important regulator of blood calcium levels. Much smaller populations of oxyphil cells, often clustered, are sometimes also present in parathyroid glands, more commonly in older individuals. They are larger than principal cells and characterized by strongly eosinophilic cytoplasm. Oxyphil cells are probably inactive, degenerated derivatives of chief cells.

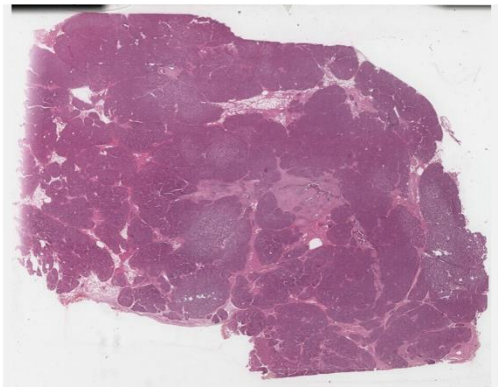
9.6 Endocrine pancreas #1



The slide exhibits sections of pancreas, which comprises an exocrine component (compound serous acinar gland) and an endocrine component. The endocrine pancreas is represent by pancreatic islets (islets of Langerhans) that are spherical masses of endocrine cells scattered throughout the acinar exocrine tissue of the pancreas. Most islets are 100-200 µm, constituting approximately 1-2% of the pancreas total volume. A very thin reticular capsule envelops each islet, separating it from the adjacent acinar tissue. The islets cells are polygonal or rounded, smaller, and more lightly stained than the surrounding acinar cells, arranged in cords, and accompanied by fenestrated capillaries. The major cell types of pancreatic islets are:

- α (A) cells – secrete glucagon
- ß (B) cells – the most numerous, secrete insulin
- δ (D) cells – secrete somatostatin
- PP (F) cells – secrete pancreatic polypeptide.

9.7 Endocrine pancreas #2



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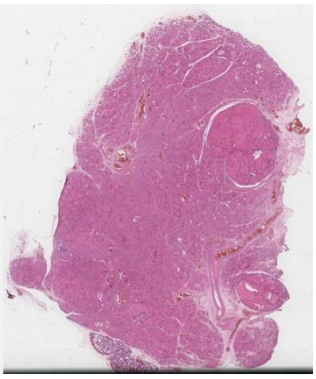
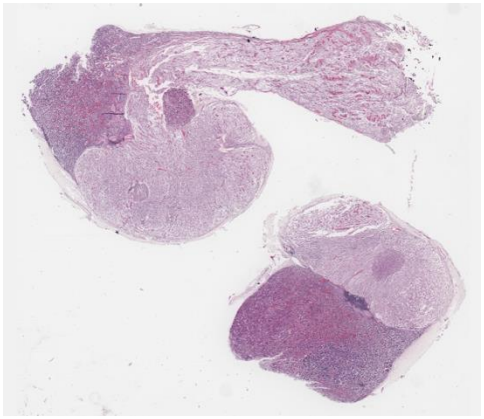
9.8 Thyroid follicular nodular disease (multinodular goiter)



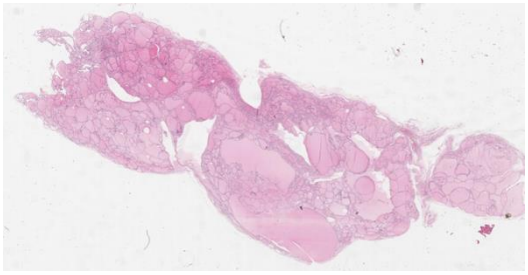
The slide shows thyroid and a fragment of parathyroid. The thyroid fragment contains three well-delimited nodules, without a thick capsule, of different diameters, made up by variable sized dilated follicles with flattened epithelium, added to microfollicular pattern, without significant cytological atypia. There are aggregates of small follicles at poles of large colloid follicles (Sanderson polster). There is a relative compression of the non-nodular thyroid tissue.

9.9 Pituitary gland #2



The slide contains the pituitary gland, which is composed of an anterior part (adenohypophysis) and a posterior part (neurohypophysis) that is directly attached to the hypothalamus region of the brain by an infundibular stalk. The adenohypophysis consists of a large pars distalis (anterior lobe), mainly seen in this section, the pars tuberalis (cranial part) and thin pars intermedia adjacent to the pars nervosa. The neurohypophysis contains large pars nervosa and infundibulum stalk that is attached to the hypothalamus at the median eminence. Pars distalis consists of cords of cells with different staining affinities (chromophils and chromophobes) surrounded by fenestrated capillaries and supporting reticular connective tissue. Chromophils include basophils and acidophils, named for their affinities for basic and acidic dyes, respectively. The chromophobes are virtually unstained. Pars intermedia is a narrow zone laying between the pars distalis and the pars nervosa; contains basophils, chromophobes, and colloid-filled cysts of various sizes derived from the lumen of the embryonic hypophyseal pouch. Pars nervosa is composed of elongated glial cells known as pituicytes. These cells appear to support numerous unmyelinated nerve fibers traveling from the hypothalamus via the hypothalamo-hypophyseal tract. Neurosecretory materials pass along these nerve fibers and are stored in expanded regions at the termination of the fibers, which are referred to as Herring bodies. Pars nervosa also contains a rich network of blood vessels, mainly fenestrated capillaries.

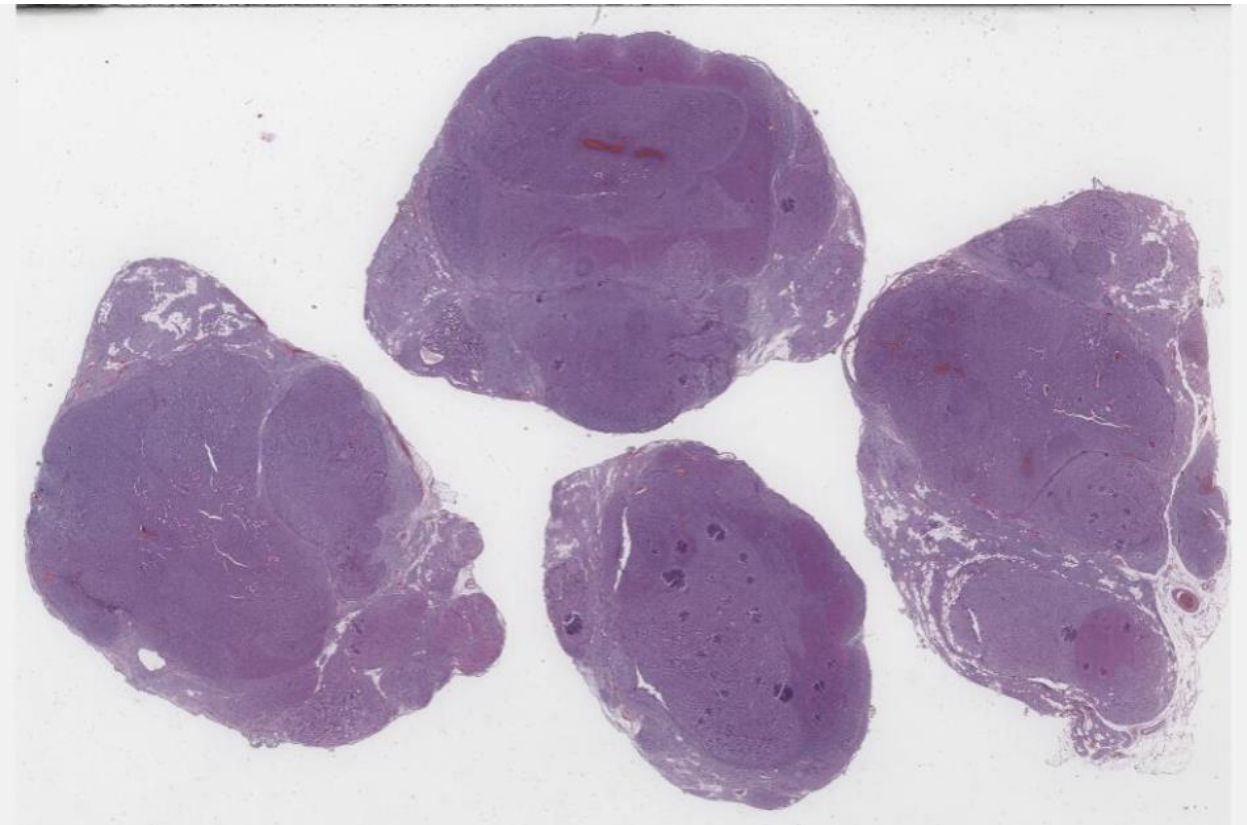
9.10 Thyroid gland



The slide shows the thyroid gland, enveloped by a capsule of fibro-elastic connective tissue, which gives rise to fine collagenous septa breaking gland into lobules. The parenchyma of the thyroid contains millions of rounded thyroid follicles of variable diameter, each lined by simple epithelium of thyrocytes (follicular cells) and central lumen densely filled with gelatinous acidophilic colloid (composed of large protein called thyroglobulin). Follicles are separated from one another by sparse reticular connective tissue. Thyroid stroma is well vascularized with fenestrated capillaries. The shape of thyrocytes (follicular cells) is controlled by thyroid-stimulating hormone (TSH) and varies from squamous to low columnar. Thyrocytes rest on a basal lamina and exhibit round and centrally located nuclei, abundant rough endoplasmic reticulum (rER), Golgi complexes, secretory granules, numerous phagosomes, lysosomes, and microvilli. They secrete thyroid hormones – T3 and T4 to adjacent capillaries. The parafollicular cells (C cells) may be found inside the basal lamina of the follicular epithelium or as isolated

clusters between follicles. They are usually larger than follicular cells and stain less intensely. Numerous, small secretory granules of C cells contain calcitonin.

9.11 Multinodular parathyroid gland hyperplasia



CHAPTER 10 - Oral cavity and Digestive tract

The digestive system is a highly intricate and dynamic system responsible for the breakdown of food into nutrients that the body can absorb and use for energy, growth, and repair. It involves a complex series of organs, each with specialized functions. In general, the digestive system can be divided into hollow organs (with a lumen) and solid organs (glandular organs) that assist in digestion. The largest structure of the digestive system is the gastrointestinal (GI) tract.

The oral cavity is the first part of the digestive tract and plays a crucial role in the initial mechanical and chemical processing of food. These include the lips, cheeks, teeth, tongue, hard and soft palate, and salivary glands. The major salivary glands include the parotid, submandibular, and sublingual glands. There are also numerous smaller minor salivary glands scattered throughout the oral cavity.

The hollow organs serve as conducts through which food or gastric chyme pass during the process of digestion. These include the esophagus, stomach, small and large intestine. The hollow organs of GI tract contain four layers: the innermost layer or the mucosa, the submucosa underneath the mucosa, followed by the muscularis propria and adventitia or serosa, as the outermost layer. These four-layered organization of the digestive tract is a histological characteristic adapted to its specific functional features.

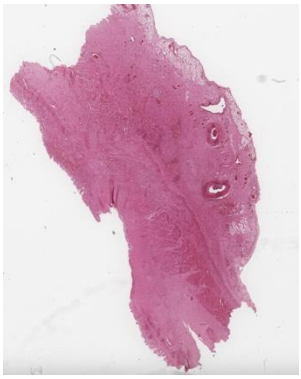
Esophagus is a muscular tube that connects the pharynx to the stomach. Esophagus is lined with stratified squamous epithelium to protect it from abrasion.

Stomach is a J-shaped, muscular organ that performs both mechanical digestion (by churning food) and chemical digestion (through gastric juice). The stomach lining simple columnar epithelium contains rugae (folds) that allow expansion after meals.

Small intestine is composed of the duodenum, jejunum, and ileum, being the primary site of digestion and absorption of nutrients. The mucosa of the small intestine exhibits some folds, named intestinal villi. Small intestine lining is made up of simple columnar epithelium with two key cell types: enterocytes (columnar cells with microvilli on their surface), forming the brush

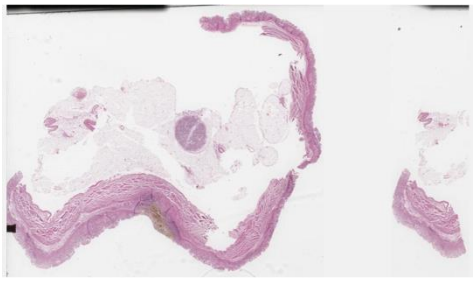
border, and goblet cells, which secrete mucus to lubricate the intestinal lining and protect it from acidic chyme and digestive enzymes.
Large intestine includes the cecum, appendix, colon (ascending, transverse, descending, and sigmoid), and rectum, being devoid of intestinal villi.
This virtual library section illustrates the histological features of the digestive system, as a preliminary step in understanding the histopathological features of the non-tumoral and tumoral lesions that involve the digestive system organs.

10.1 Peptic ulcer #1



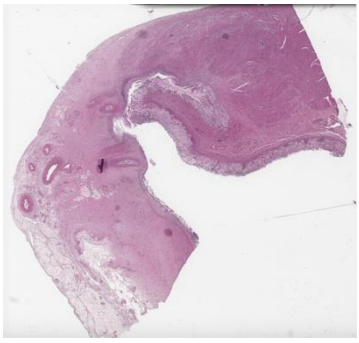
The slide shows the antrum with an ulcer involving mucosa and submucosa, with its base represented by fibrous tissue, associated with active and chronic inflammation. The surface is covered by necrotic debris and neutrophils. There is added fibrinoid necrosis, granulation tissue, thrombi, and thickened blood vessels exhibiting endarteritis obliterans.

10.2 Peptic ulcer #2



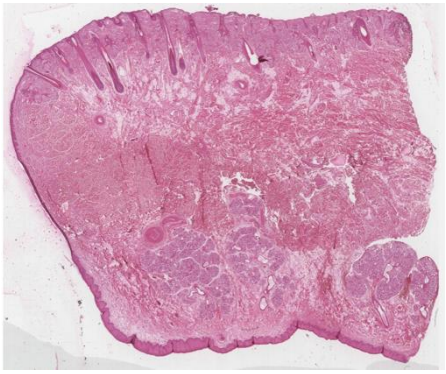
The slide shows a large stomach ulceration, extending up to submucosa, covered by fibrino-purulent debris, with neutrophils and abundant hemosiderin pigment. There is also an associated inflammatory infiltrate, with granulation tissue. The lesion is accompanied by fibrous tissue and hyalinization at the base and margins, with vessels thickening (endarteritis obliterans).

10.3 Peptic ulcer acute phase



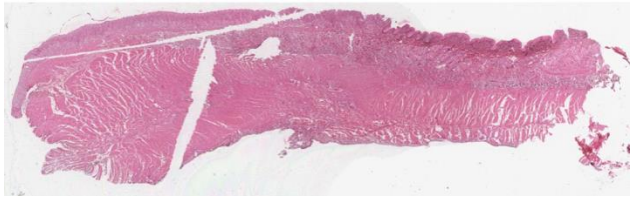
The slide shows the antrum region with an ulcer involving mucosa and, focally, submucosa. The base is represented by fibrous tissue, associated with active and chronic inflammation. The surface is covered by necrotic debris and abundant neutrophils. There is added fibrinoid necrosis, granulation tissue, thrombi, and thickened blood vessels exhibiting endarteritis obliterans.

10.4 Lip



The outer component of the lip consists of skin featuring a thin epidermis (keratinized stratified squamous epithelium), supported by dermis containing eccrine sweat glands, sebaceous glands, and hair follicles. The skin is connected to the vermillion zone (free border), distinguished by its red color, being lined by keratinized and parakeratinized stratified squamous epithelium, with deep and richly vascularized connective tissue papillae. The mucocutaneous junction marks the transition to the inner component of the lip (oral mucosa), which is lined by non-keratinized stratified squamous epithelium, supported by lamina propria and submucosa, containing multiple minor muco-serous salivary glands (labial glands). The central component of the lip is the orbicularis oris muscle, a striated skeletal muscle.

10.5 Esophagus and gastro-esophageal junction

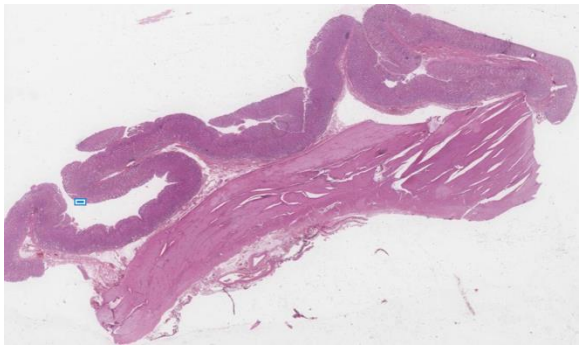


The slide shows a section of esophagus (right), a muscular tube composed of the four layers' characteristic of the gastrointestinal tract. Mucosa is comprised of non-keratinized stratified squamous epithelium, lamina propria, of connective tissue, and muscularis mucosae, composed of a longitudinal thin layer of smooth muscle interrupted by esophageal glands. Submucosa is a connective tissue, containing esophageal mucus-secreting glands with ducts lined by simple cuboidal, simple columnar, and stratified cuboidal epithelium. Muscularis externa, disposed in inner circular and outer longitudinal layers, contains skeletal muscle in the upper third, admixed with smooth muscle in the middle third (as seen in this section), and only smooth muscle in the lower third. Serosa is composed of connective tissue lined by mesothelium. There is also the gastroesophageal junction or cardioesophageal junction, as the boundary between the esophagus (right) and the cardiac region of the stomach (left). In this region, both esophagus and stomach are composed of the four layers' characteristic of the gastrointestinal tract, as the layers are continuous across the gastroesophageal junction. Mucosal lining epithelium is abruptly changed, from esophageal non-keratinized stratified squamous epithelium to simple columnar gastric epithelium, with gastric pits and cardial mucus-secreting glands situated on both sides of the junction.

10.6 Esophagus

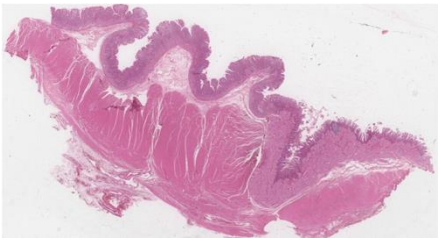
The slide shows a cross section of esophagus, a muscular tube composed of the four layers' characteristic of the gastrointestinal tract. Mucosa is comprised of non-keratinized stratified squamous epithelium, lamina propria, of connective tissue, and muscularis mucosae, composed of a longitudinal thin layer of smooth muscle interrupted by esophageal glands. Submucosa is a connective tissue, which may contain, mainly in the middle of esophagus length, esophageal mucus-secreting glands with ducts lined by simple cuboidal, simple columnar, and stratified cuboidal epithelium. Muscularis externa, disposed in inner circular and outer longitudinal layers, contains skeletal muscle in the upper third (as seen in this section), admixed with smooth muscle in the middle third, and only smooth muscle in the lower third. Adventitia is composed of loose connective tissue continuous with serosa in the sub-diaphragmatic region.

10.7 Stomach - fundic region



The slide shows a fragment of the fundic region of the stomach. Mucosa is composed of surface cells lining the gastric pits, containing mucinogen granules in the apical pole and fundic (gastric) glands. Gastric glands are tubular glands, lined by several cell types: mucous neck cells, smaller, lightly stained cells, parietal or marginal cells, large, round, with eosinophilic cytoplasm, and chief (pepsinogenic) cells, as darker staining cells, more numerous at the glands' base. Additionally, enteroendocrine cells, as small, pale staining cells, are disposed at the base of the gland. Muscularis mucosae is composed of an inner circular and an outer longitudinal thin layers of smooth muscle cells. Submucosa is a connective tissue and muscularis externa contains smooth muscle cells in the circular and longitudinal layers, focally supplemented by a third inner oblique layer. Serosa is covering the entire organ.

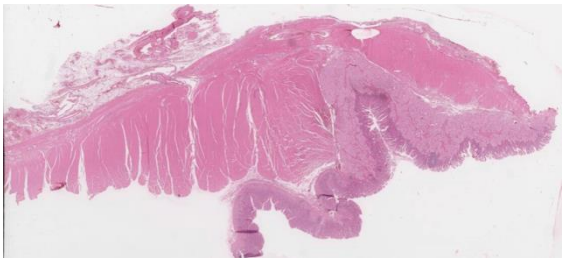
10.8 Duodenum #1



The slide shows a specimen of duodenum, which is composed of four layers. Folds of mucosa and submucosa form plicae circulares. Mucosa has slender finger-like intestinal villi lined by simple columnar epithelium, with enterocytes (absorptive cells) and mucus-secreting goblet cells. Intestinal (Lieberkuhn) crypts or simple tubular glands are found at the base of villi. Muscularis mucosae is discontinuous due to focal extensions of

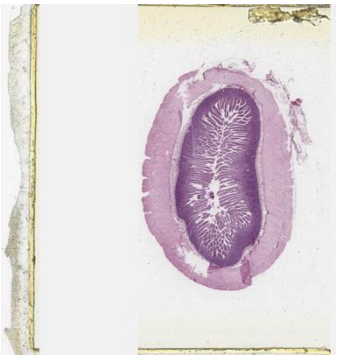
submucosal Brunner's glands, which secrete an alkaline mucus. Muscularis externa is composed of two layers of smooth muscle (inner circular and outer longitudinal). Serosa is covering the organ.

10.9 Duodenum #2



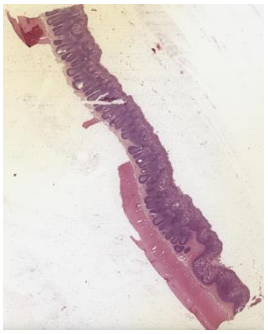
The slide shows a specimen of duodenum, which is composed of four layers. Folds of mucosa and submucosa form plicae circulares. Mucosa has slender finger-like intestinal villi lined by simple columnar epithelium, with enterocytes (absorptive cells) and mucus-secreting goblet cells. Intestinal (Lieberkuhn) crypts or simple tubular glands are found at the base of villi. Their bases contain stem cells, along with Paneth cells, with evident eosinophilic granules of lysozyme. Lamina propria may contain elements of the mucosa-associated lymphatic tissue (MALT). Muscularis mucosae is discontinuous due to focal extensions of submucosal Brunner's glands, which secrete an alkaline mucus. Auerbach’s myenteric nervous plexus is seen between the two layers of muscularis externa (inner circular and outer longitudinal). Serosa is covering the organ.

10.10 Jejunum



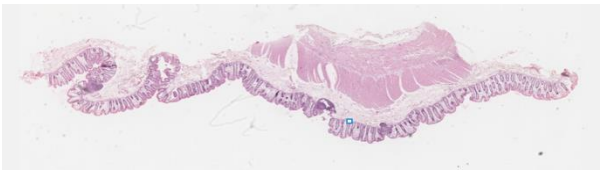
The slide shows the jejunum histology which presents four layers: mucosa, submucosa, muscularis propria (muscularis externa), and serosa. Mucosa consists of simple columnar epithelium with enterocytes and goblet cells, lamina propria (loose connective tissue) and muscularis mucosae. Surface mucosa is vastly increased via evaginating villi. Mucosa also contains short, straight, simple tubular glands (intestinal glands), commonly called Lieberkühn crypts. The submucosa is a layer of connective tissue containing blood vessels, lymphatic vessels, and nerves. The muscularis externa consists of two layers of smooth muscle: an inner circular layer and an outer longitudinal layer. Serosa is composed of connective tissue and mesothelium.

10.11 Ileum



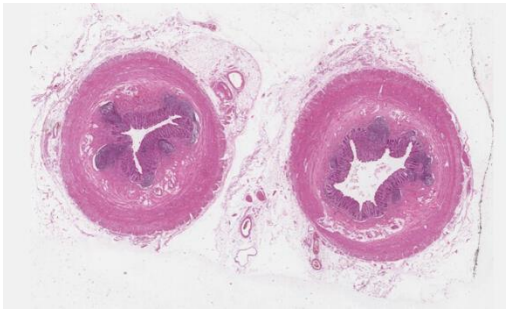
The slide shows the ileum histology comprising four layers: mucosa, submucosa, muscularis propria (muscularis externa), and serosa. Mucosa consists of simple columnar epithelium with enterocytes and goblet cells, lamina propria (loose connective tissue), and muscularis mucosae. In addition, mucosa consists of conspicuous patches of lymphoid tissue, called Peyer's patches, which may protrude into the lumen and also extend into the submucosa. Mucosa also contains short, straight, simple tubular glands (intestinal glands), commonly called Lieberkühn crypts. Surface mucosa is vastly increased via evaginating villi. The muscularis externa consists of two layers of smooth muscle: an inner circular layer and an outer longitudinal layer. Serosa is composed of connective tissue and mesothelium.

10.12 Colon



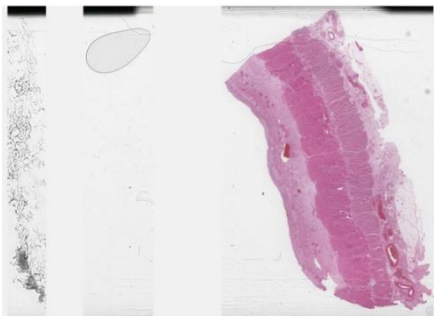
The slide shows a fragment of a colon, composed of the four characteristic layers of the gastrointestinal tract. Mucosa lacks villi or plicae circulares and displays regularly arranged crypts (Lieberkuhn glands), composed of enterocytes and numerous goblet cells, separated by a lamina propria of loose connective tissue, with focal mucosa-associated lymphatic tissue (MALT) elements. Muscularis mucosae, composed of smooth muscle, submucosa, composed of connective tissue, containing the submucosal Meissner's nervous plexus, and muscularis externa, with inner circular and outer longitudinal layers of smooth muscle, along with myenteric Auerbach's nervous plexus are also seen. The outer muscle layer is consolidated into three distinct bundles of smooth muscle (tinea coli), in humans (partially seen in this slide).

10.13 Appendix #1



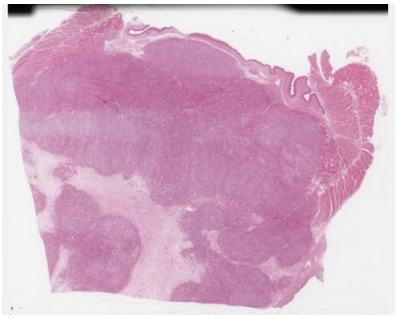
The slide shows a cross section of an appendix, which is composed of the four characteristic layers of the gastrointestinal tract. Mucosa is comprised of simple columnar epithelium, without plicae circulares or villi, containing enterocytes and goblet cells. Crypts are shorter and fewer than in colon, lamina propria has numerous lymph nodules, and muscularis mucosae is discontinuous. Submucosa may also contain lymph nodules extended from lamina propria. Muscularis externa comprises two thin layers of smooth muscle (inner circular and outer longitudinal) and the outer layer is represented by serosa.

10.14 Acute erosive esophagitis



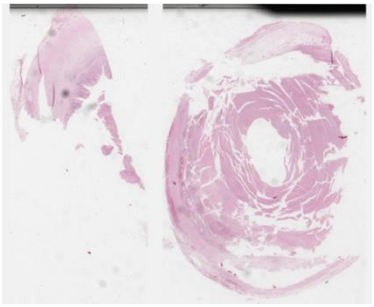
The slide shows extensive erosion of the esophageal mucosa. Lamina propria contains an abundant inflammatory infiltrate, composed of neutrophils, lymphocytes, and macrophages. The inflammation is focally extended to submucosa. Lamina propria blood vessels show congestion, alternating with hyperemia, and thrombi formation. There are also focal hemorrhages.

10.15 Esophagus infiltrative adenocarcinoma



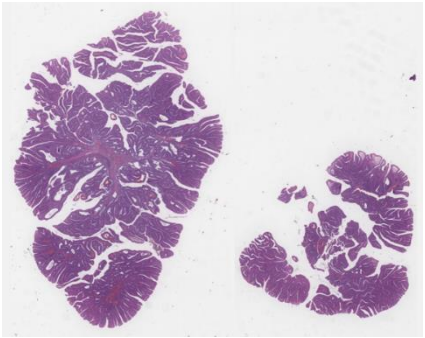
The slide shows an infiltrative adenocarcinoma, moderately differentiated, invading the external part of the esophagus wall, with dissociation of the esophageal muscularis proper, and extending up to submucosa. The esophageal mucosa is not involved by the tumor, suggesting that the tumor might be secondary. There is also evidence of vascular invasion, added to perineural invasion.

10.16 Appendicitis



The slide shows acute inflammatory infiltrate, with predominance of neutrophils that involves all layers of the appendiceal wall. There are also mucosal erosions, scattered crypt abscesses and serosal inflammation (peritonitis).

10.17 Tubulovillous colon adenoma

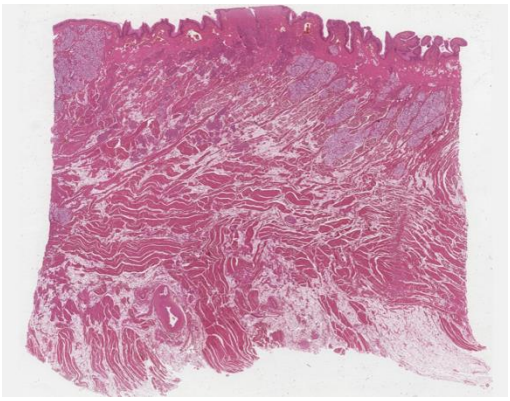


The slide shows a tubulovillous adenoma. This lesion is a benign, premalignant neoplasm, composed of dysplastic colorectal epithelium, with conserved crypt architecture, along with variable elongation of the crypts and an increased number of glands. There is a low grade dysplasia of epithelium (loss of cell polarity, hyperchromatic nuclei, along with nuclear spindling and stratification). There is a decreased amount of goblet cells and absorptive cells. The villous component displays a feature resembling small intestinal villi, representing 25 - 75% of the adenoma.

10.18 Appendix #2

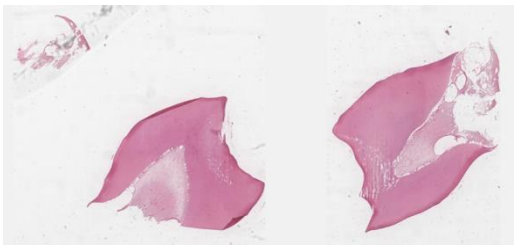
The slide shows a cross section of an appendix, which is composed of the four characteristic layers of the gastrointestinal tract. Mucosa is comprised of simple columnar epithelium, without plicae circulares or villi, containing enterocytes and goblet cells. Crypts are shorter and fewer than in colon, lamina propria has numerous lymph nodules, and muscularis mucosae is discontinuous. Submucosa may also contain lymph nodules extended from lamina propria. Muscularis externa comprises two thin layers of smooth muscle (inner circular and outer longitudinal) and the outer layer is represented by serosa.

10.19 Tongue



The slide shows the tongue components. The ventral surface is covered by oral mucosa, containing non-keratinized stratified squamous epithelium and loose connective tissue, while the dorsal surface is covered by a specialized mucosa that contains multiple types of papillae and taste buds. There are foliate papillae, as parallel ridges on the lateral edges, delimited by deep mucosal furrows, fungiform (mushroom-shaped) papillae, and circumvallate papillae, in a V-shape row, surrounded by deep clefts, receiving the secretion of serous salivary glands (von Ebner's glands), all these being covered by non-keratinized stratified squamous epithelium. There are also filiform papillae, as conical projections covered by keratinized stratified squamous epithelium, Taste buds are elliptical pale structures found in the epithelium of the foliate and circumvallate papillae or in the nearby epithelium, that contain cells with taste receptors. There is also central skeletal muscle, arranged in three bundles at right angles to each other, associated with adipose cells. Additionally, minor salivary glands are dispersed throughout the tongue.

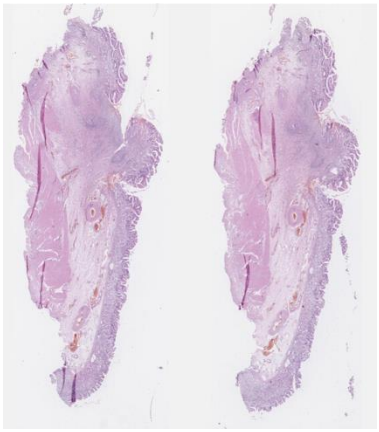
10.20 Tooth - demineralized (decalcified) section #1



The slide shows the dentin and dental pulp, each with distinct histological features and functions. Dentin contains dentinal tubules that host odontoblasts processes, which extend from the pulp-dentin interface to the dentin-enamel or dentin-cementum junctions.

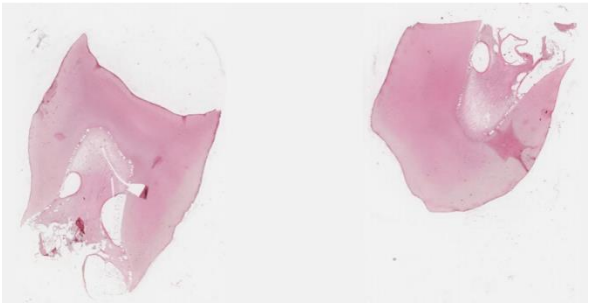
The dental pulp is made up of loose connective tissue, is surrounded by dentin and is lined by odontoblasts along the pulp-dentin interface. The pulp contains blood vessels, nerves, and many connective tissue cells, along with lymphoid cells.

10.21 Stomach - pyloric region



The pyloric region of the stomach is composed of the four layers' characteristic for the digestive tract. Mucosa is composed of epithelium, lamina propria, and muscularis mucosae. Gastric pits, as surface invaginations, are lined with surface mucous cells and are very deep, often extending more than halfway to the muscularis mucosae. Pyloric glands appear as cross-sections of short, branched tubular glands of only mucous-secreting cells that empty into the bottom of gastric pits. Lamina propria consists of small amounts of connective tissue found between pits and glands. Muscularis mucosae consists of thin layers of smooth muscle cells. Submucosa is made of connective tissue. Muscularis externa has two layers of smooth muscle cells, with a markedly thickened inner circular layer forming the pyloric sphincter. Serosa is covering the organ.

10.22 Tooth - demineralised (decalcified) section #2

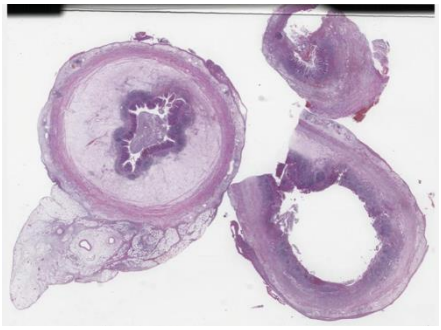


The slide shows the dentin-pulp complex. Dental pulp is formed by loose connective tissue, that contains stromal fibroblasts, that are in the center of the pulp and constitute the most abundant pulp cell population. In addition, odontoblasts are the second type of pulp cells, that are situated in the peripheral area. Numerous capillaries and nerves are also located in the dental pulp. Dentin contains dentinal tubules, in which the processes of odontoblasts are located. Dentinal tubules are thin tubes running radially from the pulp of the tooth to the enamel or cementum.

10.23 Tooth - ground section

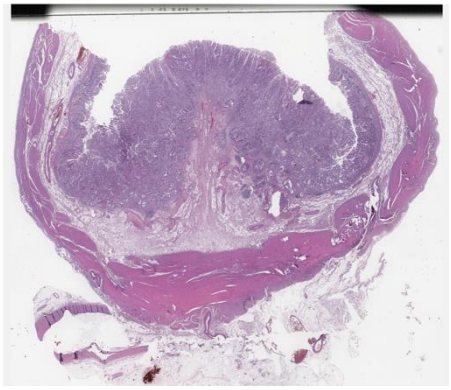
The slide shows the ground section of dentin and enamel, along with the dentin-enamel junction, as the border between enamel and dentin. Note the branching ends of the odontoblastic processes, seen here in the mantle dentin, just under the dentin-enamel junction. Enamel contains: enamel lamellae (the structure passing from the surface of the enamel to the dentin-enamel junction), enamel tufts, enamel spindles, and stria of Retzius, easily identified in this slide.

10.24 Acute phlegmonous appendicitis



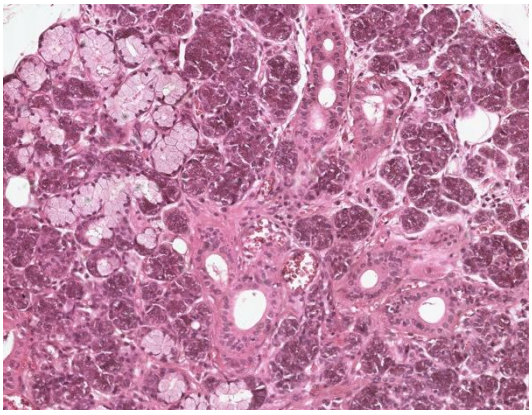
The slide shows acute inflammatory infiltrate, with predominance of neutrophils that involves all layers of the appendiceal wall. There are also mucosal erosions and ulcerations, scattered crypt abscesses, luminal collections of neutrophils, edema, and serosal inflammation (peritonitis).

10.25 Gastric tubular adenocarcinoma



The slide shows infiltrative gastric adenocarcinoma (low-grade) with predominant tubular pattern. Gastric adenocarcinoma exhibits subtle architectural changes, with irregularly fused glands, nuclear enlargement (high nuclear to cytoplasmic ratio), stratification and hyperchromasia, associated with desmoplastic stroma and intratumoral necrosis. Tumor exhibits muscularis mucosae and submucosa layers infiltration. The mucosa non-involved by the tumor shows intestinal metaplasia.

CHAPTER 11 - Glands of digestive tract



The digestive tract contains intrinsic glands which are situated in mucosa or submucosa and associated glands that are releasing their secretory products into the digestive tract, facilitating its specific functions. The solid organs of the digestive system do not process food directly through a lumen but produce and secrete substances essential for digestion.

The salivary glands consist of three pairs of major glands: parotid, submandibular, and sublingual glands. Along with these major glands, there are also minor salivary glands, scattered throughout the oral cavity. Inflammation of the salivary glands is often caused by infections (viral or bacterial), autoimmune diseases, or obstruction of the ducts (due to stones, i.e., sialolithiasis). The most common malignant salivary gland tumour is mucoepidermoid carcinoma, followed by adenoid cystic carcinoma. These tumours have highly infiltrative nature and frequently grow along nerve sheaths, a process called perineural invasion.

The liver is composed of functional units called lobules, where blood from the digestive tract is filtered through sinusoids lined by specialized cells (hepatocytes) that perform metabolic functions. In the normal liver, reticulin fibers stained with Gomori's silver, form a fine, organized reticular framework around hepatocytes and liver sinusoids, reflecting the arrangement of hepatocytes in hepatic lobules. Reticulin staining helps in the grading and staging of fibrosis, in liver pathology.

Hepatic steatosis, or fatty liver disease, is characterized by the accumulation of fat in hepatocytes. It is typically classified into non-alcoholic or alcoholic fatty liver disease.

Cirrhosis represents the end stage of chronic liver disease, being characterized by irreversible scarring (fibrosis) and altered liver architecture, leading to liver dysfunction and hepatocytes death. Fibrosis is associated with the formation of characteristic regenerative nodules.

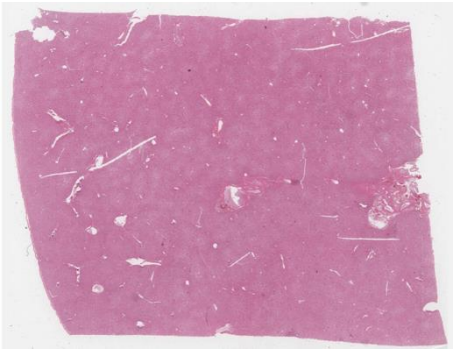
The most common benign liver tumour is hepatic hemangioma, while the most common primary liver cancer, often associated with cirrhosis and chronic hepatitis B/C infection is hepatocellular

carcinoma. Cholangiocarcinoma is a malignancy of the bile ducts, often associated with primary sclerosing cholangitis or parasitic infections, in endemic areas.

The gallbladder is a small, hollow pear-shaped organ, covered by the peritoneum, which has in the innermost layer a mucosa lined by simple columnar epithelium with microvilli. Smooth muscle and serosa are the next layers. It may be also involved in inflammatory and tumoral processes.

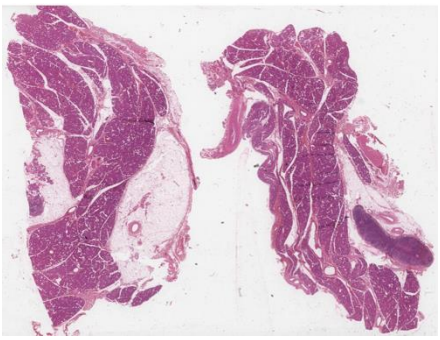
The pancreas is a mixed gland, having both exocrine and endocrine functions. The exocrine portion produces digestive enzymes (amylase, lipase, and proteases, like trypsin) that are secreted into the duodenum through the pancreatic duct. These enzymes breakdown carbohydrates, fats, and proteins, while the endocrine portion, made up of the islets of Langerhans, secretes hormones, like insulin and glucagon, which regulate blood sugar levels. Like all solid organs, pancreas contains three components: capsule, stroma and parenchyma. The most common and highly aggressive form of cancer is pancreatic ductal adenocarcinoma, while neuroendocrine tumors that arise from the hormone-producing cells of the pancreas are known as insulinoma and gastrinoma.

11.1 Liver #1



The slide shows a parenchymal organ lined by a dense irregular connective tissue capsule (Glisson's capsule) sending septa, which divide the liver into lobes and lobules. The classic liver lobule is a roughly hexagonal structure, although poorly delimited, containing a central vein and about three portal triads at its periphery, in humans. The central vein is a relatively large venule situated in the center of the lobule, surrounded by hepatocytes and sinusoidal capillaries. Hepatocytes are disposed in anastomosing plates, one or two cell thick, which radiate around the central vein. Sinusoidal capillaries are situated between plates of hepatocytes and are lined by endothelial cells and Kupffer cells. Portal triads are situated at the corners of lobules, being composed of connective tissue supporting a hepatic arteriole, a portal venule, and an interlobular bile duct, lined by a simple cuboidal epithelium. Variable lymphatic vessels, capillaries, and nerves may be also associated to the portal triads.

11.2 Parotid gland

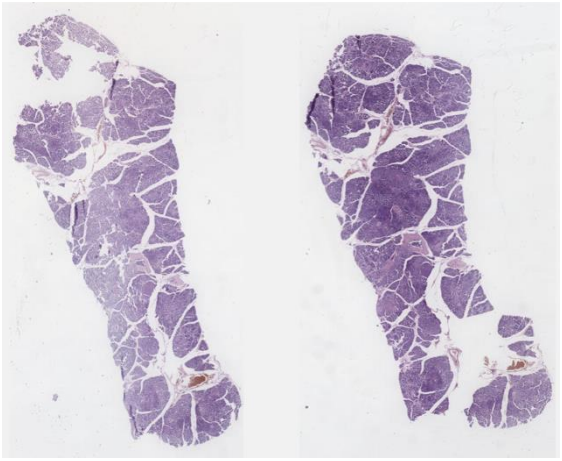


The slide shows a major pure serous salivary gland. The gland is surrounded by a dense irregular connective tissue capsule, sending septa that divide the gland into lobules and contains a loose connective tissue stroma, associated with white adipose cells. Parenchyma consists of secretory cells disposed in serous acini, with protein-secreting, dark basophilic cells, with round nuclei. Intralobular ducts are intercalated ducts, corresponding to individual acini, lined by simple low cuboidal epithelium and striated ducts, lined by simple columnar epithelium with basal striations. Interlobular (extralobular or excretory) ducts are disposed in the connective tissue septa and are lined by pseudostratified, stratified cuboidal or stratified columnar epithelium.

11.3 Mixed salivary gland - submandibular gland

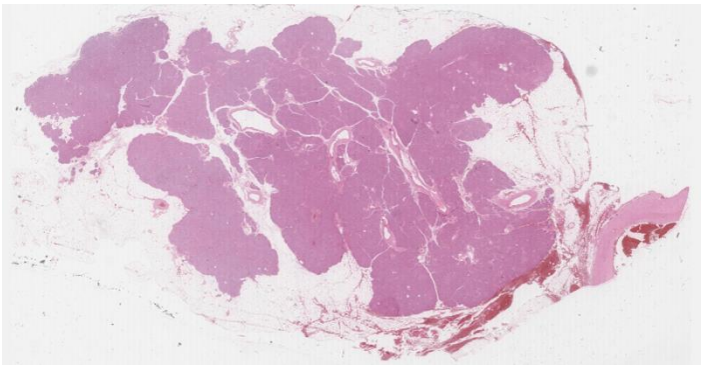
The slide shows a major mixed salivary gland, which is mostly serous, while its mucous component is minor. The gland is surrounded by a dense irregular connective tissue capsule, sending septa that divide the gland into lobules and contains a loose connective tissue stroma. Parenchyma consists of secretory cells disposed in acini or tubes, with serous (protein-secreting) dark basophilic cells, with round nuclei and mucous pale cells, with flattened nuclei. Crescents of Giannuzzi (demilunes of Heidenhain) are composed of serous cells, being disposed as a cap on mucous cells. Intralobular ducts are intercalated ducts, corresponding to individual acini, lined by simple low cuboidal epithelium and striated ducts, lined by simple columnar epithelium with basal striations. Interlobular (extralobular or excretory ducts) are disposed in the connective tissue septa and are lined by pseudostratified, stratified cuboidal or stratified columnar epithelium.

11.4 Pancreas #1



The slide shows the pancreas, which is a mixed exocrine (around 98% exocrine component) and endocrine gland (1-2% endocrine component). The capsule is made up of connective tissue that sends thin septa that divide the organ into lobules. The stroma is loose connective tissue with blood vessels, nerves, and nervous microganglia. Parenchyma is represented by serous acini with centroacinar cells (duct cells situated within acini) and intralobular ducts (intercalated ducts, lined by simple cuboidal epithelium). Interlobular ductsare located outside lobules and are lined by simple columnar, stratified columnar or stratified cuboidal epithelium, being supported by a thick layer of connective tissue. Islets of Langerhans(endocrine pancreas) are round-ovoid, scattered, lightly stained clusters of endocrine cells cords, with capillaries between the cords.

11.5 Pancreas #2

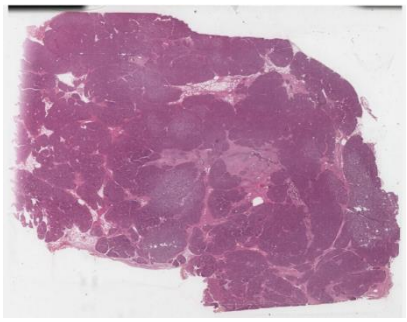


The slide shows the pancreas, which is a mixed exocrine (around 98% exocrine component) and endocrine gland (1-2% endocrine component). The capsule is made up of connective tissue that sends thin septa that divide the organ into lobules. The stroma is loose connective tissue with blood vessels, nerves, and nervous microganglia. Parenchyma is represented by serous acini with centroacinar cells (duct cells situated within acini) and intralobular ducts (intercalated ducts, lined by simple cuboidal epithelium). Interlobular ducts are located outside lobules and are lined by simple columnar, stratified columnar or stratified cuboidal epithelium, being supported by a thick layer of connective tissue. Islets of Langerhans (endocrine pancreas) are round-ovoid, scattered, lightly stained clusters of endocrine cells cords, with capillaries between the cords.

11.6 Pancreas #3

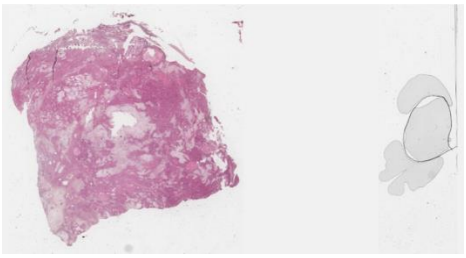
The slide shows the pancreas, which is a mixed exocrine (around 98% exocrine component) and endocrine gland (1-2% endocrine component). The capsule is made up of connective tissue that sends thin septa that divide the organ into lobules. The stroma is loose connective tissue with

blood vessels, nerves, and nervous microganglia. Parenchyma is represented by serous acini with centroacinar cells (duct cells situated within acini) and intralobular ducts (intercalated ducts, lined by simple cuboidal epithelium). Interlobular ducts are located outside lobules and are lined by simple columnar, stratified columnar or stratified cuboidal epithelium, being supported by a thick layer of connective tissue. Islets of Langerhans (endocrine pancreas) are round-ovoid, scattered, lightly stained clusters of endocrine cells cords, with capillaries between the cords.



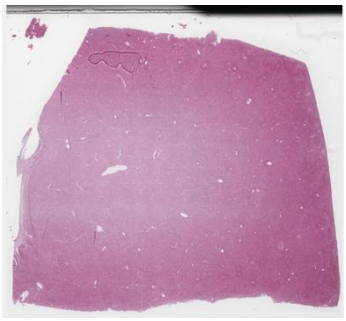
11.7 Pleomorphic adenoma of the parotid gland #1

The slide shows a circumscribed, encapsulated tumor with two components: epithelial (ductal) and stromal (dominant). Epithelial components form the inner cystic layer. Stromal components are typically myxoid, chondroid or myxochondroid. There is also a hyalinized or fibrotic area and a rim of normal parotid gland.



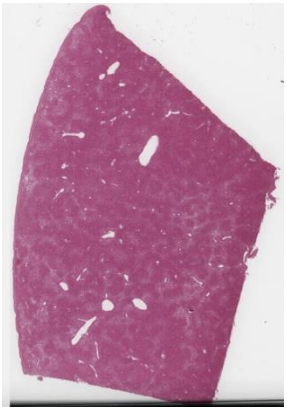
11.8 Liver steatosis - mixed (microvesicular and macrovesicular) pattern

The slide shows fat accumulation in hepatocytes with a mixed pattern. This pattern associates macrovesicular steatosis, as large droplets, displacing the nuclei, and microvesicular steatosis, as small droplets, representing progressive phases in fat storage into hepatocytes. The portal spaces contain the triads associated with a mononuclear infiltrate. There are also congested sinusoidsbetween hepatocytes cords.

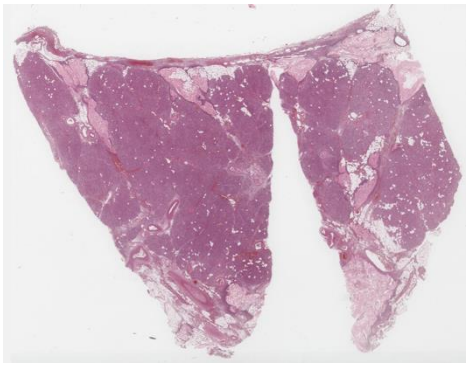


11.9 Granulomatous hepatitis

The slide shows the presence of multiple small epithelioid granulomas, composed of aggregates of epithelioid macrophages and occasional multinucleated giant cells. There is no evidence of caseating central necrosis characteristic for Mycobacterium tuberculosis granuloma. The liver parenchyma also shows chronic inflammatory infiltrate in portal spaces.

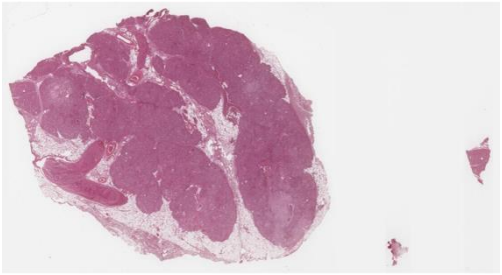


11.10 Acute interstitial pancreatitis



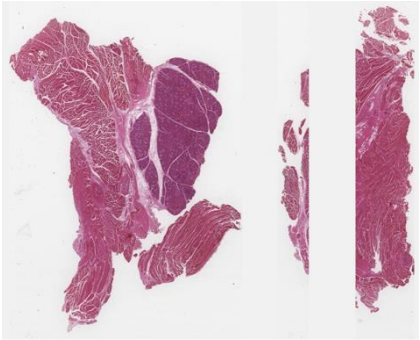
The slide shows acute inflammatory infiltrate with preservation of the pancreatic lobular parenchyme, containing serous acini and ducts. There is also a lymphocytic and plasma cells infiltrate, parenchyme edema and interstitium edema. Additionally, fat necrosis of peripancreatic tissues is also noticed, with lipid laden macrophages and anucleate, light eosinophilic (ghost) cells.

11.11 Acute necrotising pancreatitis (hemorrhagic pancreatitis)



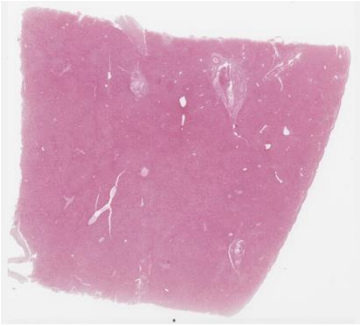
The slide shows extensive hemorrhage involving the pancreatic lobules, thrombosis, with panlobular coagulative necrosis, and lack of intact nuclei, with some lobules still discernible. There are also neutrophils admixed with macrophages and lymphocytes. Additionally, fat necrosis of peripancreatic tissues is also noticed.

11.12 Viral sialadenitis with CMV (Cytomegalovirus)



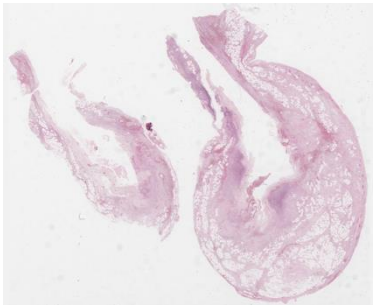
The slide shows interstitial edema, intense hyperemia, and a dense lymphohistiocytic infiltrate. There are also characteristic intranuclear "owl's eye" viral inclusions in ducts and acini. Another feature of viral sialadenitis is the lack of acute inflammation.

11.13 Chronic passive congestion of the liver



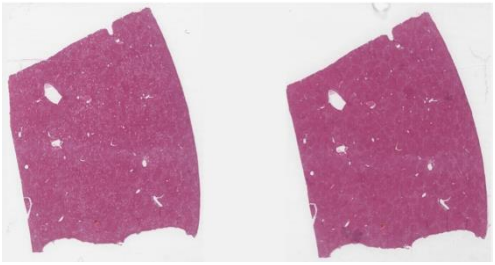
The slide is showing dilated central veins and dilated sinusoids, with compression of hepatocytes, with discrete central hemorrhagic necrosis due to ischemia. Focal mediolobular fatty change (macrovesicular and microvesicular steatosis) is also noticed, while periportal hepatocytes are not involved.

11.14 Gangrenous cholecystitis



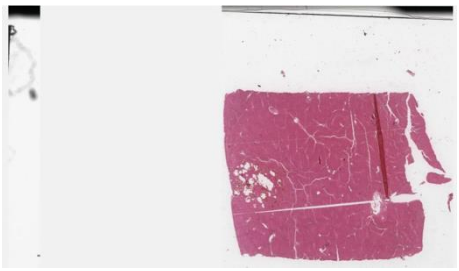
The slide shows gallbladder wall thickening, with transmural acute inflammation, along with ischemic necrosis, edema, and hemorrhages. The lumen exhibits erosions, with focal sloughed mucosa, and intraluminal membranes. There are also fibrin deposits on the serosa surface.

11.15 Chronic hepatitis



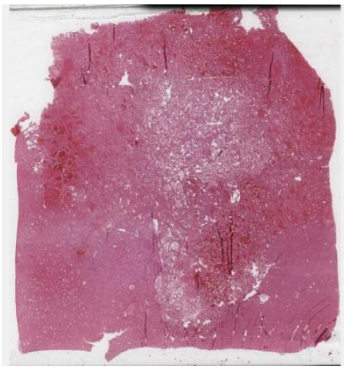
The slide shows progressive fibrosis of the limiting plate resulting in enlargement of portal tracts and stellate periportal fibrous extension, added to portal - portal fibrous bridging or portal - central fibrous bridging. There is also portal inflammation made up of mononuclear infiltrate (lymphocytes and few plasma cells). Additionally, there is an interface hepatitis or piecemeal necrosis, with hepatocytes apoptosis and inflammation at the parenchymal-stromal interface, with lymphocytic infiltrate. Focal lobular hepatitis comprised of mononuclear infiltrate of the hepatic lobules and occurrence of necrotic or apoptotic hepatocytes (Councilman bodies) may be also seen. There is also a diffuse mixed pattern steatosis.

11.16 Cavernous hepatic hemangioma #1



The slide shows a circumscribed vascular proliferation, containing variably sized, dilated blood vessels lined by a single layer of flat endothelial cells, without cytologic atypia or mitosis, and variable wall thickness. The vascular spaces are separated by fibrous septa, with focal hyalinization. The interface with the surrounding hepatic parenchyma is irregular and contains a focal leukocyte infiltrate.

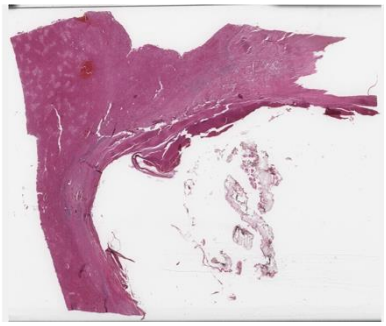
11.17 Cavernous hepatic hemangioma #2



The slide shows a large poorly circumscribed vascular proliferation, containing variably sized, dilated, focally congested blood vessels lined by a single layer of flat endothelial cells, without cytologic atypia or mitosis, and variable wall thickness. The vascular spaces are separated by fibrous septa, with focal hyalinization. The

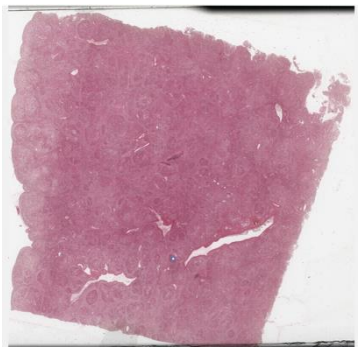
interface with the surrounding hepatic parenchyma is irregular and contains a focal leukocyte infiltrate. The remnant liver parenchyma shows microvesicular steatosis.

11.18 Liver hydatid cyst



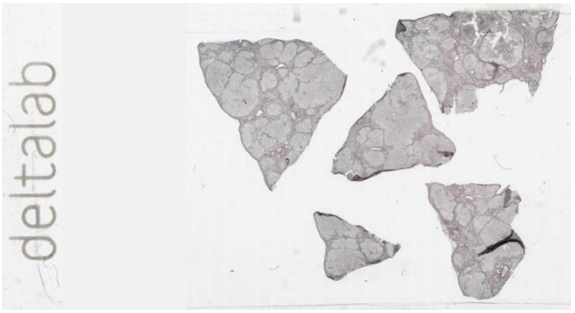
The slide shows the presence of a liver cyst, composed by an outer acellular laminated membrane and a germinal membrane. The inner content is represented by attached protoscolices with a round-ovoid shape containing hooklets and a sucker. Around the hydatid cyst, there is an evident fibrotic layer, with chronic inflammation.

11.19 Liver micronodular cirrhosis



The slide shows a complete replacement of normal hepatic architecture with small rounded regenerative parenchymal nodules, with loss of normal central – portal relationship (of portal spaces, central veins, and radial pattern of hepatocytes). The nodules contain mixed steatosis (fatty change), macrovesicular and microvesicular types. There are relatively thick bridging fibrous septa, associated with variable chronic inflammatory infiltrate (lymphocytes and macrophages), surrounding the nodules.

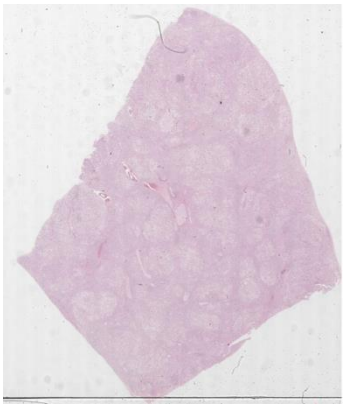
11.20 Liver - reticulin fibers staining



The slide shows a reticulin stain of the liver. There are reticulin anastomosing fibers, stained in black, within capsule and septa, supporting the hepatocytes plates and sinusoids, around the central vein, and around the components of the portal triads.

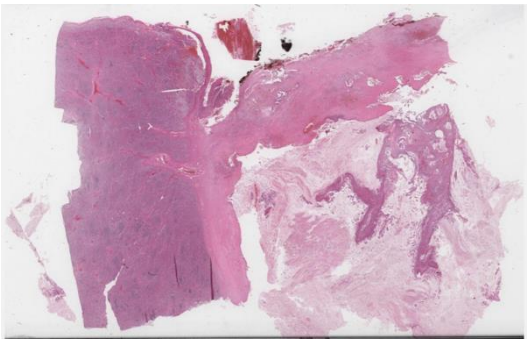
11.21 Liver #2

The slide shows a parenchymal organ lined by a dense irregular connective tissue capsule (Glisson's capsule) sending septa, which divide the liver into lobes and lobules. The classic liver lobule is a roughly hexagonal structure, although poorly delimited, containing a central vein and about three portal triads at its periphery, in humans. The central vein is a relatively large venule situated in the center of the lobule, surrounded by hepatocytes and sinusoidal capillaries. Hepatocytes are disposed in anastomosing plates, one or two cell thick, which radiate around the central vein. Sinusoidal capillaries are situated between plates of hepatocytes and are lined by endothelial cells and Kupffer cells. Portal triads are situated at the corners of lobules, being composed of connective tissue supporting a hepatic arteriole, a portal venule, and an interlobular bile duct, lined by a simple cuboidal epithelium. Variable lymphatic vessels, capillaries, and nerves may be also associated to the portal triads.



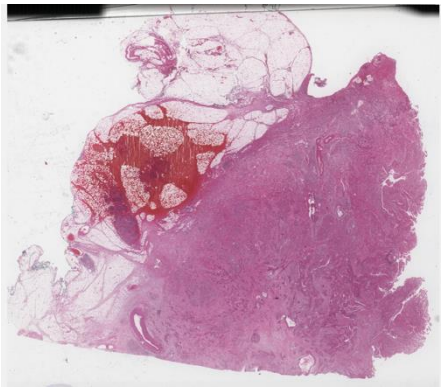
11.22 Mucinous neoplastic cyst (MCN) of the pancreas associated with invasive ductal adenocarcinoma

The slide shows a multilocular cysts, located in the pancreatic tail, with adhesions to the splenic capsule, lined by gastric epithelium with variable atypia, of low and high grade, that also contains ovarian type stroma. Well differentiated ductal structures, lined by mild pleomorphic cuboidal epithelium are identified in the splenic capsule.

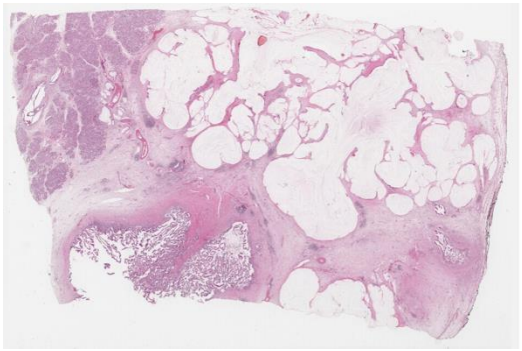


11.23 Adenosquamous carcinoma of the pancreas

The slide shows pancreatic parenchyma with glandular structures lined by stratified pleomorphic epithelium (adenocarcinoma component) and non-ductal areas, composed of nests or sheets of cells with focally marked nuclear atypia, intracellular keratinization and apparent intercellular bridges (extensive squamous component). Additionally, perineural invasion of the squamous component can be noticed.

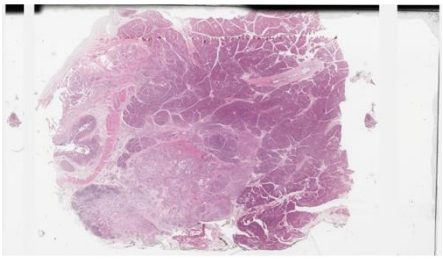


11.24 Intraductal papillary mucinous neoplasm (IPMN) associated with colloid carcinoma of the pancreas



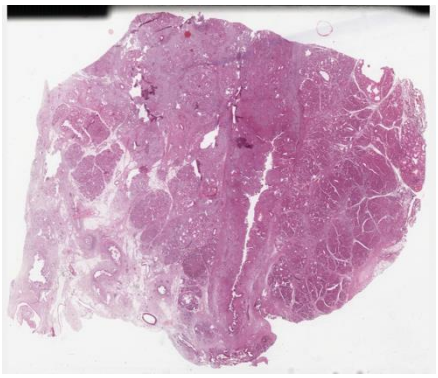
The slide shows large extracellular mucin pools with low cellularity, some of them partially lined by low cuboidal epithelium or with few suspended cells, in the vicinity of cystic structures with prominent papillae, lined by low and high grade atypical epithelium with intestinal features. There is also remnant pancreatic parenchyma uninvolved by neoplasia.

11.25 Pancreatic ductal adenocarcinoma (PDAC) NOS



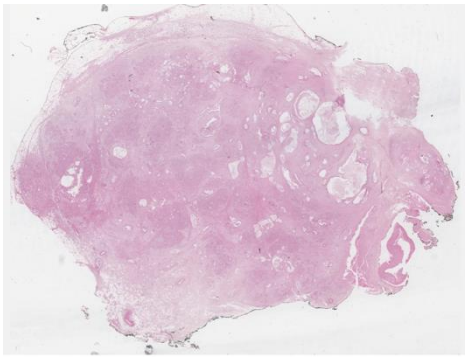
The slide shows normal pancreatic parenchyma containing a heterogenous ductal proliferation composed of cells with marked nuclear atypia, arranged in classic angulated glandular ducts, cribriform structures, and micropapillary areas. The tumoral cells invade the duodenum muscularis externa, loco-regional lymph nodes, vessels, and nervous structures.

11.26 Pancreatic ductal adenocarcinoma associated with pancreatic intraductal neoplasia (PanIN)



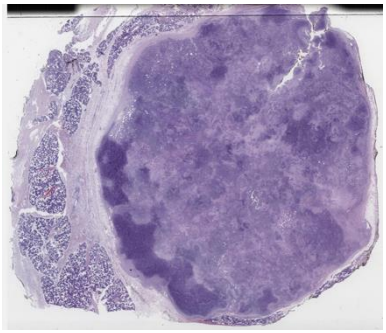
The slide shows medium sized duct with carcinoma in situ – carcinoma invasive sequence, composed of classic/conventional ductal adenocarcinoma that spreads haphazardly around a muscular artery and through the connective tissue septa. The pancreatic parenchyma contains extensive or lobular pancreatic intraepithelial neoplasia (PanIn) with low grade features, associated with acinar-to-ductal metaplasia, but also tumor intraductal spread - HG PanIn mimicry (duct cancerization).

11.27 Pancreatic ductal adenocarcinoma - foamy gland pattern



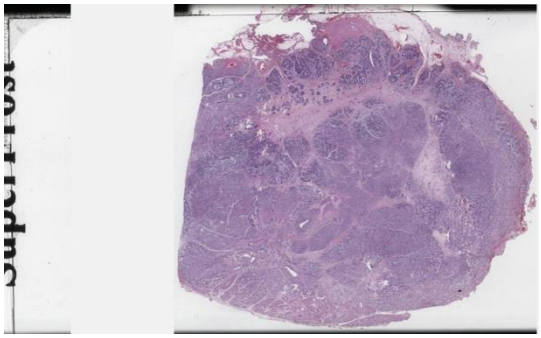
The slide shows normal pancreatic parenchyma and haphazardly distributed well-formed glands, with deceptive benign appearance, composed of columnar cells with abundant cytoplasm, eosinophilic brush-border like apical staining and basal oriented raisinoid nuclei. There is also perineural invasion and vascular invasion ("orphan artery sign").

11.28 Pleomorphic adenoma of the parotid gland #2



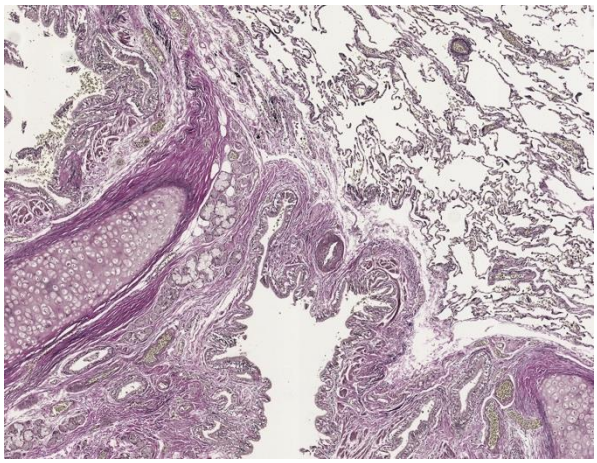
The slide shows a well demarcated, bosselated, encapsulated tumor with two components: epithelial (ductal) and stromal chondroid component (dominant). Epithelial components form the inner cystic layer and exhibits preserved myoepithelial cells. Stromal components are typically myxoid, chondroid or myxochondroid. There is also a hyalinized or fibrotic area and a rim of normal parotid gland.

11.29 Adenoid cystic carcinoma of the salivary gland



The slide shows a large tumor with tubular, cribriform, and solid architecture, composed of ductal and myoepithelial cells with dark angulated nuclei and scanty cytoplasm, giving a basaloid appearance. Ductal cuboidal cells with eosinophilic cytoplasm and areas with cribriform pattern are also visible. There are also myxoid or hyalinized globules. Perineural invasion is also noticed.

CHAPTER 12 - Respiratory System



The respiratory system provides oxygen and carbon dioxide exchange between the inhaled air and the blood. It includes the lungs and air passages represented by a branched system of bronchial tubes that links the sites of gas exchange with the external environment. From an anatomical point of view, the respiratory conducting tract is divided into structures of the upper and lower parts. Functionally, the respiratory system includes:

- a conducting portion, which contains the nasal cavities, nasopharynx, larynx, trachea, bronchi, bronchioles, and terminal bronchioles;

- a respiratory portion involved in gas exchange, consisting of respiratory bronchioles, alveolar ducts, and alveoli.

This system performs three main functions: filtration, conduction of air, and gas exchange. In addition, the conducting part of the respiratory system changes the air temperature to the body temperature and moisturises it to have the proper humidity level, protects the body from harmful substances by coughing, supports the smell and phonation functions, and converts the angiotensin I to angiotensin II.

Most of the conducting system is covered by respiratory epithelium that includes two main cell types: ciliated and goblet cells. Goblet cells produce mucus that traps particulate matter from the air, whilst the ciliated cells have surface cilia that move the thin mucus layer containing the trapped particles. This structure is associated with an extensive blood vessel network, situated beneath the epithelium, that warms the air and seromucous glands in the submucosa, which participate in the air moistening.

The wall of the trachea and large bronchi includes hyaline cartilage rings. These become irregular cartilage plates in smaller branches.

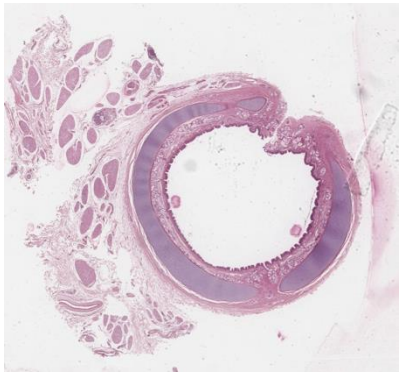
Smooth muscle tissue is also a pivotal component of the respiratory conducting system wall, which is able to modify the diameter of the airway and, therefore, the airflow, particularly in those air passages with less cartilage.

Alveoli, the cellular sites of the exchange of gases between inspired air and blood, are sac-like structures, lined by alveolar epithelium. Type I alveolar cells that cover most of the alveolar surface are involved in gas exchanges. Type II alveolar cells secrete a surface-active material called surfactant, which reduces alveolar surface tension, preventing alveolar collapse during exhale.

The respiratory epithelium may be affected by inhaled chemical toxins, viruses, and bacteria. In addition, viral infections may increase the vulnerability to secondary bacterial infections. The bronchial tree is also a significant site for lung carcinoma development, often originating in areas of squamous metaplasia of the bronchial mucosa, in heavy smokers.

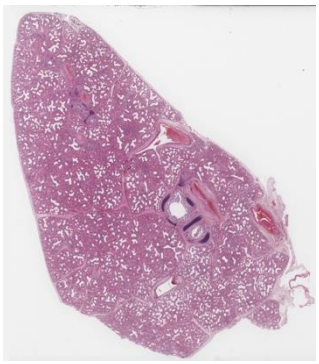
This virtual library section illustrates the histological features of the lungs and the conducting part of the respiratory system, as a preliminary step in understanding the histopathological features of the non-tumoral and tumoral lesions that involve the respiratory system components, such as bronchogenic cyst, bronchopneumonia, lung tuberculosis, lung infarct, silicosis, pulmonary emphysema, lung hamartoma, and lung carcinoma.

12.1 Trachea #1



The trachea is a thin-walled tube with three layers. Tunica interna is lined with a typical respiratory mucosa, with pseudostratified columnar ciliated epithelium. Lamina propria is rich in elastic fibers and lymphoid follicles, while seromucous tracheal glands are found in the submucosal layer (tela submucosa). Sixteen to 20 C-shaped rings of hyaline cartilage are found in the tunica media. The open ends of the rings are located on the posterior surface of the trachea. A fibroelastic ligament and bundles of smooth muscle (trachealis muscle) bind to the perichondrium and bridge the open ends of these C-shaped cartilages. Tunica adventitia is composed of loose connective tissue with blood vessels and nerves.

12.2 Fetal lung



The slide show potential air spaces, which are small, almost completely lined by a sort of cuboidal epithelium and separated from one another by broad and cellular walls. The presence of developing bronchi and bronchioles and respiratory regions, with alveolar ducts and alveoli are also noticed. Alveolar ducts arise from respiratory bronchioles, as passageways lined with simple cuboidal epithelium and relatively few alveoli – small spherical or duct-like structures.

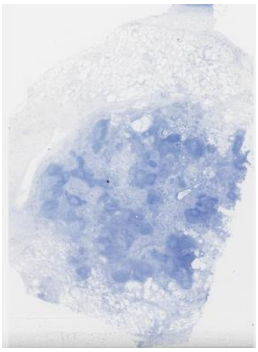
12.3 Trachea #2

The trachea is a thin-walled tube with three layers. Tunica interna is lined with a typical respiratory mucosa, with pseudostratified columnar ciliated epithelium. Lamina propria is rich in elastic fibers and lymphoid follicles, while seromucous tracheal glands are found in the submucosal layer (tela submucosa). Sixteen to 20 C-shaped rings of hyaline cartilage are found in the tunica media. The open ends of the rings are located on the posterior surface of the trachea. A fibroelastic ligament and bundles of smooth muscle (trachealis muscle) bind to the perichondrium and bridge the open ends of these C-shaped cartilages. Tunica adventitia is composed of loose connective tissue with blood vessels and nerves.

12.4 Trachea #3

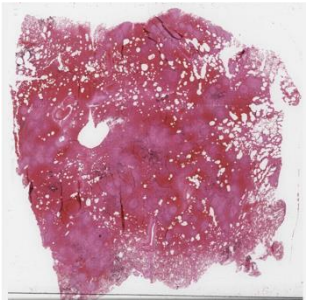
The trachea is a thin-walled tube with three layers. Tunica interna is lined with a typical respiratory mucosa, with pseudostratified columnar ciliated epithelium. Lamina propria is rich in elastic fibers and lymphoid follicles, while seromucous tracheal glands are found in the submucosal layer (tela submucosa). Sixteen to 20 C-shaped rings of hyaline cartilage are found in the tunica media. The open ends of the rings are located on the posterior surface of the trachea. A fibroelastic ligament and bundles of smooth muscle (trachealis muscle) bind to the perichondrium and bridge the open ends of these C-shaped cartilages. Tunica adventitia is composed of loose connective tissue with blood vessels and nerves.

12.5 Lung tuberculosis - Ziehl-Neelsen staining



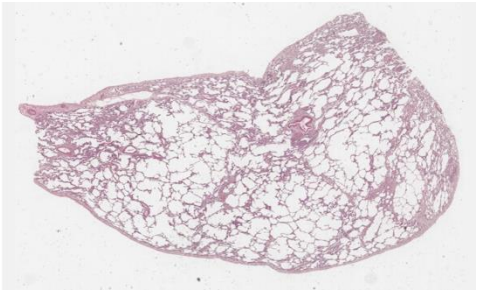
The slide shows lung multiple rounded granulomas. Using a larger magnification, a focal positive Ziehl-Neelsen staining (AFB stain) of Koch bacilli (bright red or pink) may be observed, supporting the diagnosis of lung tuberculosis.

12.6 Lung tuberculosis - H&E staining #1



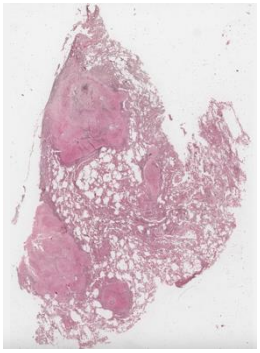
The slide shows a necrotizing granulomatous inflammation, with numerous granulomas. Tuberculoid granulomas consist of a central necrotic zone surrounded by epithelioid histiocytes, associated with multinucleated giant cells of Langhans type (nuclei peripherally disposed in a horseshoe pattern) and lymphocytes. There are also nonnecrotising granulomas.

12.7 Pulmonary emphysema



The slide shows an abnormal enlargement of air spaces distal to the terminal bronchioles, with alveolar septa destruction, without significant fibrosis. There are added fragmented alveolar walls. There may be centracinar involvement (surounding the bronchovascular bundle), paraseptal involvement, and panacinar involvement (as seen in this slide). There may be variable degrees of inflammation.

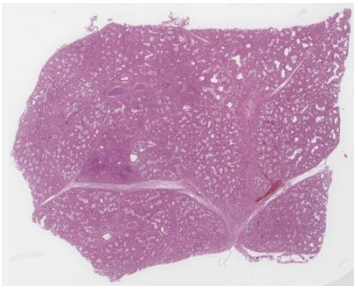
12.8 Silicosis



The slide exhibits lung fragments with nodules composed of collagen bundles, admixed with fibroblasts and histiocytes containing silica. There is marked progressive fibrosis, with hyalinized and condensed collagen, added to some cholesterol clefts. Intra-cellular and extra-cellular needle-like spicules with pointed ends, of up to 5 microns, displaying birefringce may be identified in polarized light (not shown in this type of preparation).

12.9 Acute respiratory distress syndrome (ARDS) and bronchopneumonia

The slide shows the exudative (acute) phase of diffuse alveolar damage. There are alveolar changes, with deposition of hyaline membranes in alveolar ducts and sacs walls, interstitial edema and intra-alveolar edema, and focal collapsed alveoli. Superimposed pneumonia is demonstrated by the presence of intra-alveolar fibrinopurulent exudate with neutrophils. Denudation and necrosis of type I pneumocytes is also seen. Blood vessels show necrosis of endothelial cells, intra-luminal neutrophil aggregation, microthromboemboli, and hemorrhages.

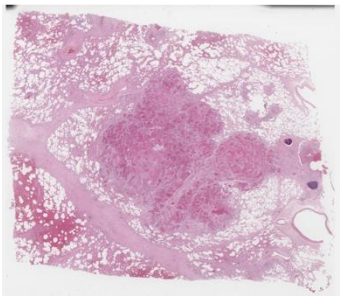


12.10 Cellular nonspecific interstitial pneumonia

The slide shows a patchyinterstitial mononuclear inflammatory infiltrate, including lymphocytes, macrophages, and occasional plasma cells. There is added focal intra-alveolar edema and focal alveolar hemorrhages.

12.11 Lung squamous cell carcinoma

The slide shows areas with well differentiated atypical squamous cells, with intercellular bridging, and focal keratinization, including keratin pearls. There is added abundant inflammation and tumor necrosis, associated with karyorrhectic debris. Mitoses are also identified.

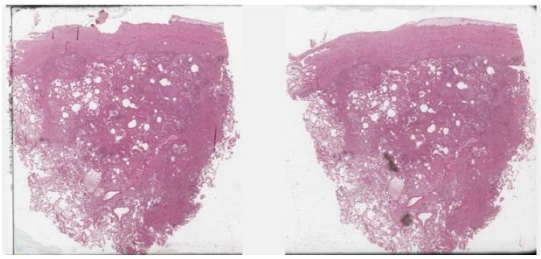


12.12 Lung infarct

The slide shows a wedge shaped subpleural zone of hemorrhage with coagulative necrosis exhibiting ischemic necrosis of the alveolar walls, bronchioles and arteries, with loss of alveolar nuclei. There is an associated large vessel antemortem throboembolus, which displays erythrocyte and fibrin layering (lines of Zahn). The thromboembolus is partially organized by migrating fibroblasts and myofibroblasts.

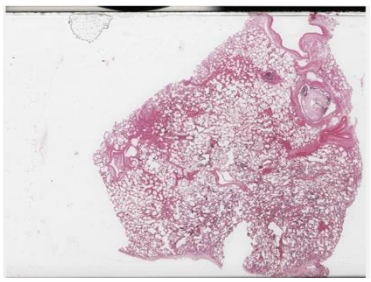
12.13 Bronchopneumonia, pleuritis, and lung squamous cell carcinoma

The slide shows vascular engorgement, patchy intra-alveolar fibrinopurulent exudate, red blood cells and focal intra-alveolar fibrin, along with fibrin deposits associated with leukocytes on the visceral pleura (pleuritis). There are added variable areas composed of squamous atypical cells (squamous cell carcinoma).



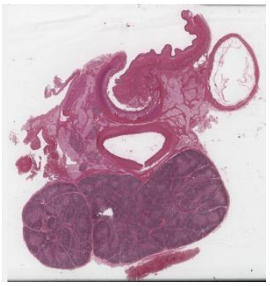
12.14 Bronchial and alveolar foreign bodies

The slide shows foreign bodies in a bronchus lumen and in alveolar spaces. Vegetal cells and striated muscle cell sections, associated with a brown-black granular material are observed in a segmental (tertiary) bronchus lumen. Focal alveolar edema is also noticed.



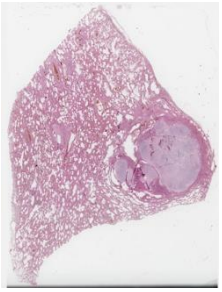
12.15 Bronchogenic cyst

The slide shows a well-delimited cystic lesion lined by respiratory-type epithelium. The cyst is partially filled with serous material. The cyst wall contains smooth muscle cells and a few serous glands in a connective tissue band.

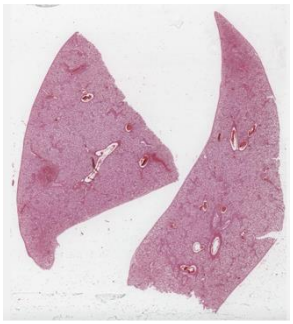


12.16 Lung hamartoma

The slide shows a relatively well-delimited tumor-like mass mainly composed of different mesenchymal tissues, with hyaline cartilage, white adipose tissue, some smooth muscle, and bone. There are also bland spindle cells and fibro-myxoid areas. These components are admixed with entrapped benign epithelial cells.

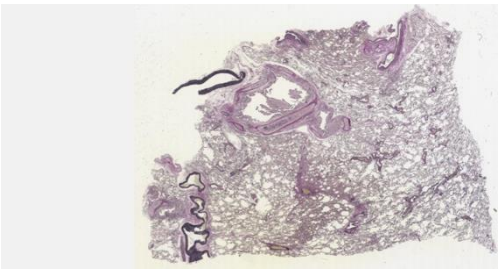


12.17 Premature newborn lung



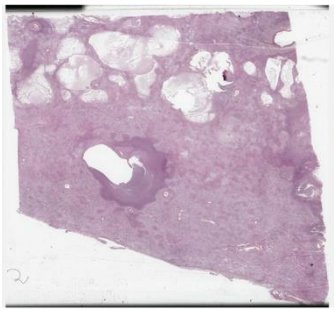
The slide contains sections involving the respiratory tract walls and alveolar spaces, associated with intense vascular congestion and focal autolysis of bronchial and bronchiolar lining epithelium. There are also areas of alveolar hemorrhages, along with numerous squames and meconium in alveolar spaces.

12.18 Lung - elastin fibers



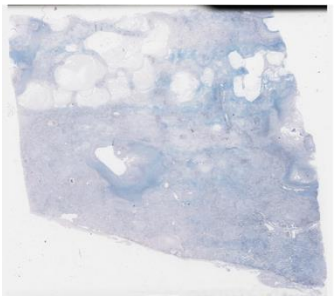
The slide shows a lung with the presence of bronchi with cartilage plates, bronchioles, and respiratory regions, as well as alveolar ducts and alveoli. Bronchioles are branches of bronchi with the smallest conducting parts, called terminal bronchioles, that finish in respiratory bronchioles. At that point, the first part of gas exchange begins. Alveolar ducts arise from respiratory bronchioles, as passageways lined with simple cuboidal epithelium that finish in alveolar sacs and alveoli. Noticed the elastin fibers black-stained.

12.19 Lung tuberculosis - H&E staining #2



The slide shows a necrotizing granulomatous inflammation, with numerous granulomas. Tuberculoid granulomas consist of a central necrotic zone surrounded by epithelioid histiocytes, associated with multinucleated giant cells of Langhans type (nuclei peripherally disposed in a horseshoe pattern) and lymphocytes. There are also nonnecrotising granulomas.

12.20 Lung tuberculosis - Ziehl-Neelsen staining #2



The slide shows lung multiple rounded granulomas. Using a large magnification, a focal positive Ziehl-Neelsen staining (AFB stain) of Koch bacilli (bright red or pink) may be observed, supporting the diagnosis of lung tuberculosis.

CHAPTER 13 - Urinary System

The urinary system filters blood, removes waste, and regulates fluid, electrolyte, and acid-base balance. It consists of the kidneys, ureters, urinary bladder, and urethra. The kidneys, as the system's primary organs, contain functional units called nephrons that perform blood filtration and urine production.

Histologically, the urinary system includes:

- Kidneys: composed of nephrons with segments like the corpuscle, proximal convoluted tubule, loop of Henle, distal convoluted tubule, associated to collecting ducts.

- Ureters and bladder: lined by transitional epithelium (urothelium) and containing variable smooth muscle layers to facilitate urine transport and storage.

- Urethra: varies in structure between genders, with transitional epithelium proximally, changing distally to stratified squamous epithelium.

The nephrons are responsible for blood filtration and reabsorption of essential substances while excreting waste. The glomerulus, situated within the corpuscle, consists of fenestrated capillaries and podocytes, forming a filtration barrier. Tubules lined by simple cuboidal epithelium reabsorb water, electrolytes, and nutrients, while the collecting ducts transport urine to the renal pelvis.

The urinary system encompasses a range of pathological conditions, from inflammatory diseases to malignancies. Glomerulonephritis involves the inflammation of glomeruli, while acute tubular necrosis (ATN) results from tubular epithelial damage due to ischemia or toxins. Interstitial nephritis is characterized by inflammatory infiltration within the renal interstitium, often linked to drug reactions or infections. Chronic kidney disease (CKD) is characterized by progressive structural changes, including glomerulosclerosis, tubular atrophy, and interstitial fibrosis.

Renal tumors are an essential aspect of urinary pathology, with renal cell carcinoma (RCC) being the most common malignant tumor of the kidney, alongside benign tumors, such as oncocytoma and angiomyolipoma. Wilms tumor or nephroblastoma, is a notable pediatric renal malignancy.

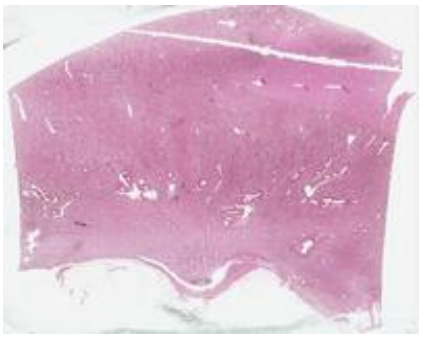
Additionally, urothelial carcinoma, originating from the transitional epithelium lining the bladder and ureters, is a frequent malignancy of the urinary tract. Arising from the transitional epithelium of the bladder, ureters, or renal pelvis, urothelial carcinoma often shows irregular, invasive growth

patterns of atypical cells with pleomorphic nuclei. It may present as either papillary or flat lesions, with high-grade tumors showing greater risk for invasion and metastasis.

Histopathological analysis of these conditions is crucial for accurate diagnosis and treatment planning. Microscopic examination, including techniques such as immunohistochemistry, allows clinicians to differentiate between tumor types and assess the extent of disease.

This chapter provides an overview of the histology and histopathological features of the urinary system, forming the basis for understanding diseases like glomerulonephritis, acute kidney injury, chronic kidney disease, along with renal and urothelial cancers.

13.1 Kidney #1

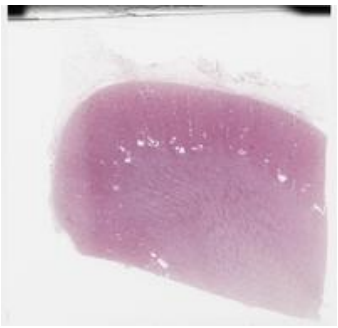


Kidney is covered by a capsule surrounded by lobules of adipose tissue. In the cortex, it comprises renal corpuscles surrounded by Bowman's capsule and containing the glomerulus associated with mesangium. Bowman’s capsule has a parietal layer of simple squamous epithelium and a visceral layer composed of podocytes. Corpuscles have a vascular pole and a urinary pole. Cortex contains numerous proximal convoluted tubules, added to scattered distal convoluted tubules. Some of distal convoluted tubules form macula densa, as a part of the juxtaglomerular apparatus. Medulla contains collecting ducts and loops of Henle. The vertical striations of medulla emanating towards cortex are named medullary rays and contain straights tubules and collecting ducts.

13.2 Kidney #2

Kidney is covered by a capsule surrounded by lobules of adipose tissue. In the cortex, it comprises renal corpuscles surrounded by Bowman's capsule and containing the glomerulus associated with mesangium. Bowman’s capsule has a parietal layer of simple squamous epithelium and a visceral layer composed of podocytes. Corpuscles have a vascular pole and a urinary pole. Cortex contains numerous proximal convoluted tubules, added to scattered distal convoluted tubules. Some of distal convoluted tubules form macula densa, as a part of the juxtaglomerular apparatus. Medulla contains collecting ducts and loops of Henle. The vertical striations of medulla emanating towards cortex are named medullary rays and contain straights tubules and collecting ducts.

13.3 Kidney #3



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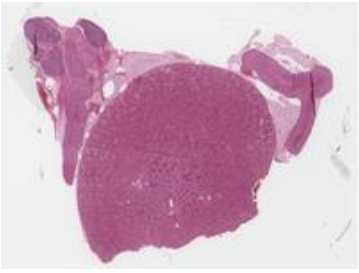
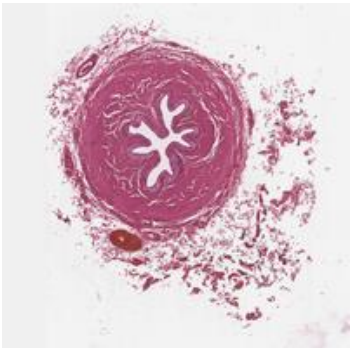
13.4 Fetal kidney



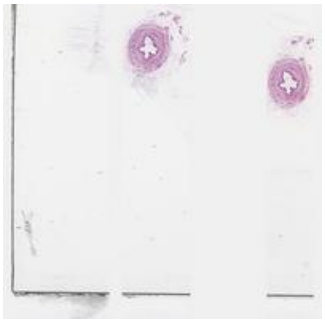
The slide shows a fetal kidney, associated with several sections through the adrenal gland, nervous ganglia, lymph nodes, and lobules of white and brown adipose tissue of the perirenal fat. The cortex contains renal corpuscles, some of them, located in the outer cortex, being developing corpuscles, in variable stages, while others are mature corpuscles, located in themature corpuscles, located in the deeper cortex. Proximal convoluted tubules are abundant in cortex, with eosinophilic cross-sections, lined by simple cuboidal to columnar epithelium with an irregular, often stellate lumen. Distal convoluted tubules are also seen, being lined by a simple cuboidal epithelium with a regular lumen outline. Medulla is composed of collecting tubules and loops of Henle.

13.5 Ureter #1



The slide shows a hollow organ lined by concentric layers: mucosa, containing transitional epithelium (urothelium) and lamina propria, muscularis externa, and adventitia. Transitional epithelium consists of several layers of cells, with superficial cells named umbrella cells, large dome-shaped, some binucleated, that change their shape depending on the distention of the ureter. Lamina propria is a thick layer of fibro-elastic connective tissue. Muscularis externa contains two layers of smooth muscle in the proximal ureter (inner longitudinal and outer circular) and three layers (inner longitudinal, middle circular, and outer longitudinal) in the distal ureter. Adventitia is a loose connective tissue with adipose tissue, blood vessels, and nerves.

13.6 Ureter #2



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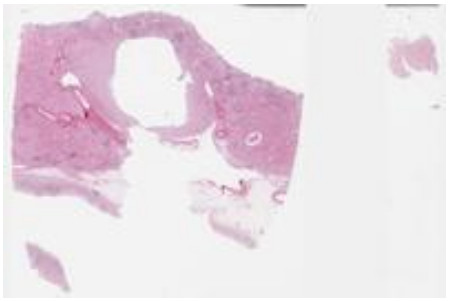
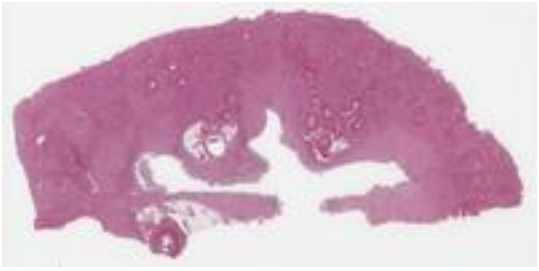
13.7 Chronic pyelonephritis



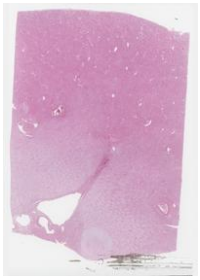
The slide shows the presence abundant interstitiallymphoplasmacytic inflammation, glomerulosclerosis, arteriolosclerosis, tubular atrophy of thyroid type, along with periglomerular and interstitial fibrosis. There is added calyx cystic dilatation.

13.8 Acute pyelonephritis



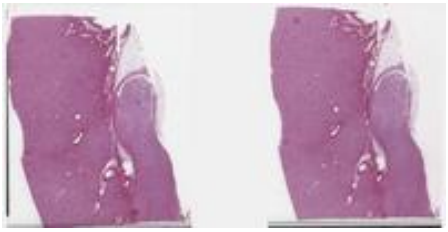
The slide shows the presence of a patchy suppurative inflammation (microabscesses), with central bacteria colonies, mainly involving the renal cortex, with abundant interstitial and intra-tubular neutrophils (neutrophil casts) and tubular necrosis. There are also cortical areas of necrosis, ischemia, and abscesses, with pus accumulation in renal calyx. The remnant renal parenchyma shows patchy lymphoplasmacytic inflammation, glomerulosclerosis, tubular atrophy of thyroid type, along with periglomerular and interstitial fibrosis, supporting a background of chronic pyelonephritis.

13.9 Reno-medullary interstitial tumor #1



The slide shows a well delimited medullary tumor, comprised of loose basophilic stroma, containing small stellate or spindle cells. Cells lack mitotic activity. There are entrapped tubules at the periphery and irregular deposits of amyloid. The surrounding kidney tissue shows glomerulosclerosis and arteriolosclerosis.

13.10 Reno-medullary interstitial cell tumor #2



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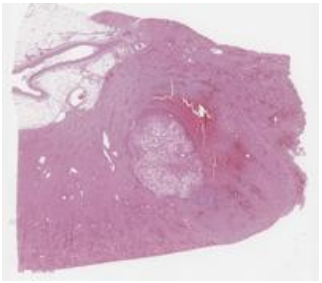
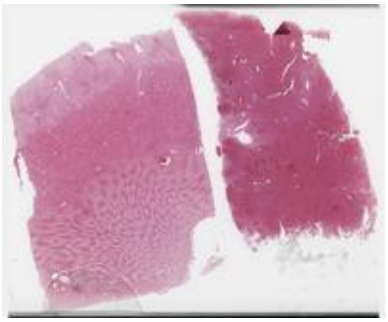
13.11 Renal angiomyolipoma



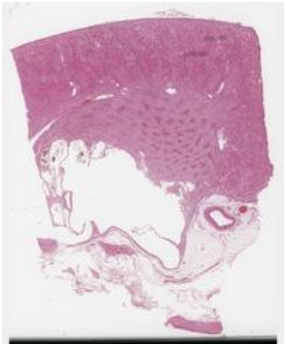
The slide shows a circumscribed, nonencapsulated renal tumor, with pushing borders, containing a triphasic pattern of growth. It is composed of mature adipose tissue, myoid spindle cells, and large pleomorphic epithelioid cells. The tumor contains entrapped renal tubules and dysmorphic thick walled hyalinized blood vessels, without elastic lamina.

13.12 Renal-adrenal fusion



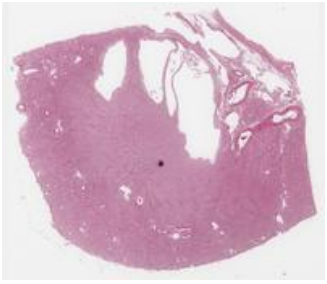
The slide shows an incidental intrarenal nodule of adrenal gland covered by renal capsule, without a fibrous capsule between adrenal and renal tissue. There are evident adrenal cortex zones (glomerulosa, fasciculata, and reticularis). Although rarely, reduced areas of adrenal medulla are also seen. The subjacent renal parenchyma shows focal glomerulosclerosis and arteriolosclerosis. A fragment of spleen has been also collected along with kidney tissue.

13.13 Renal multicystic nephroma #1



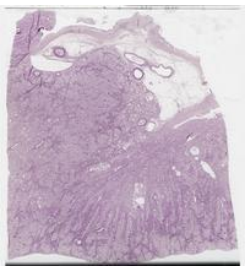
The slide shows a well delimited collection of variable sized cysts separated by septa of variable thickness. The lining epithelium is simple, either flat, cuboidal, or hobnail, with minimal atypia, and no mitoses. There are hypocellular, collagenous and fibrous septa, with some spindle cells. Some hemosiderin laden macrophages may be also seen. The surrounding renal parenchyma shows benign nephrosclerosis.

13.14 Renal multicystic nephroma #2



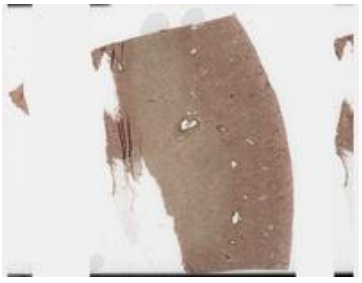
The slide shows a well delimited collection of variable sized cysts separated by septa of variable thickness. The lining is simple, either flat epithelium, cuboidal epithelium, or hobnail type, with minimal atypia, and no mitoses, foci of blunt and delicate papillae, and focal multiple layers of epithelium. The stroma tissue is associated with hypocellular, collagenous and fibrous septa, with some spindle cells. The surrounding renal parenchyma shows benign nephrosclerosis.

13.15 Diabetic kidney disease – PAS staining



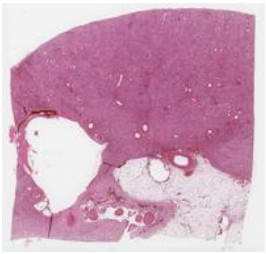
The slide shows diffuse uniform thickening of the glomerular basement membrane associated with diffuse mesangial expansion. There is added glomerulosclerosis and tubular atrophy, with thickening of the tubular basement membranes.

13.16 Diabetic kidney disease – Goldner-Szekely trichrome staining



The slide shows diffuse uniform thickening of the glomerular basement membrane associated with nodular mesangial expansion (Kimmelsteil-Wilson lesions). There is added glomerulosclerosis and tubular atrophy, with thickening of the tubular basement membranes.

13.17 Diabetic kidney disease – H&E staining

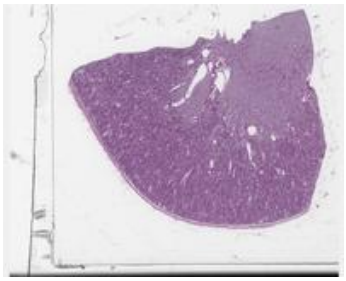


The slide shows diffuse uniformthickening of the glomerular basement membrane associated with evident nodular mesangial expansion (Kimmelsteil-Wilson lesions). Vascular hyalinosis is also seen. Large subendothelial lipohyaline deposits are visible at the periphery of the glomerular tuft (hyaline caps). There is also glomerulosclerosis and tubular atrophy, with thickening of the tubular basement membranes.

13.18 Uretero-hydronephrosis

Cross section through the kidney shows extreme dilation of the renal pelvis associated with severe atrophy of the renal parenchyma. In renal pelvis, the lining urothelium displays focal atrophy and reactive changes, with important fibrosis of the lamina propria. The renal parenchyma contains marked chronic inflammatory infiltrate, tubular atrophy, and intersititial fibrosis, along with extensive glomerulosclerosis. The pelvic adipose tissue contains the main renal vessels with significant congestion and aterosclerotic lesions.

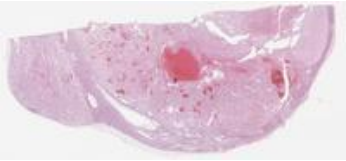
13.19 Kidney #4



Kidney is covered by a capsule surrounded by lobules of adipose tissue. In the cortex, it comprises renal corpuscles surrounded by Bowman's capsule and containing the glomerulus associated with mesangium. Bowman’s capsule has a parietal layer of simple squamous epithelium and a visceral layer composed of podocytes. Corpuscles have a vascular pole and a urinary pole. Cortex contains numerous proximal convoluted tubules, added to scattered distal convoluted tubules. Some of distal convoluted tubules form macula densa, as a part of the juxtaglomerular apparatus. Medulla contains collecting ducts and loops of Henle. The vertical striations of medulla emanating towards cortex are named medullary rays and contain straights tubules and collecting ducts.

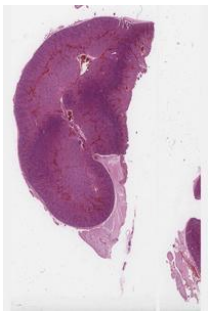
13.20 Invasive urothelial carcinoma plasmacytoid component - transurethral resection

13.21 Clear cell renal cell carcinoma



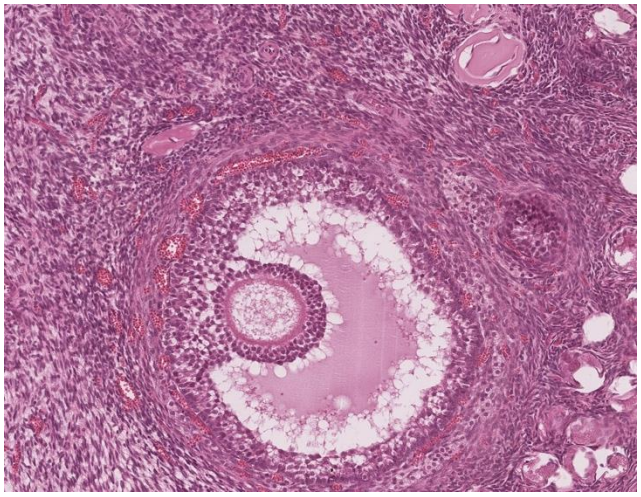
The renal parenchyma is showing an epithelial malignant proliferation consisting of round or polyhedral cells with clear, eosinophylic cytoplasm and central, pale nuclei with one or more conspicuous nucleoli (WHO/ISUP nucleolar grade 3). The tumour pattern is acinar/ alveolar, macro- and microcystic, tubular, pseudopapillary, with gracile intratumoral stroma.

13.22 Kidney development (stage 2-3 of nephrogenesis)



The slide shows sections of the kidney cortex and medulla in stages 2 to 3 of nephrogenesis. Various nephron types, such as comma-shaped or ''S'' shape, added to fetal renal corpuscles are observed in the renal cortex.

CHAPTER 14 - Female Reproductive System



The female genital system plays a crucial role in reproduction and overall health. This system includes the ovaries, fallopian tubes, uterus, cervix, and vagina, each contributing to the complex functions of reproduction, hormone regulation, and menstrual cycles. In this regard, the female genital system serves multiple vital functions:

· Reproduction: facilitates fertilization, implantation, and development of the embryo and fetus.

· Hormonal regulation: ovaries produce hormones essential for the menstrual cycle, pregnancy, and secondary sexual characteristics.

· Menstrual cycle: the cyclical shedding of the endometrial lining prepares the uterus for potential implantation of embryo.

From an anatomical perspective, the female genital system can be divided into external and internal structures, each with distinct histological characteristics.

1. External genitalia (vulva):

o Comprises the mons pubis, labia majora and minora, clitoris, and vestibular glands.

o The external structures are primarily lined by stratified squamous epithelium, which provides protection and sensory function.

2. Internal genitalia:

o Ovaries: responsible for oocyte production and hormone secretion (estrogens and progesterone). The ovarian structure includes the cortex, which contains follicles at various stages of development, and the medulla, rich in blood vessels.

o Fallopian tubes: facilitate the transport of oocytes and are lined with ciliated columnar epithelium, which aids in moving the ovum towards the uterus.

o Uterus: composed of three layers - endometrium (inner), myometrium (middle), and perimetrium (outer). The endometrium undergoes cyclical changes influenced by hormonal fluctuations, critical for implantation.

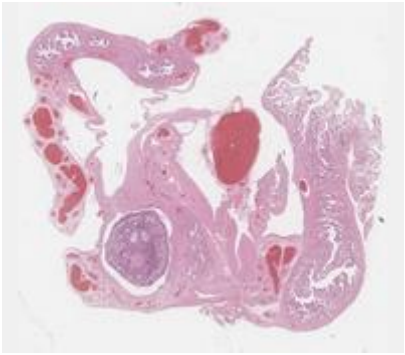
o Cervix: functions as a barrier and conduct, lined with mucus-secreting columnar epithelium, transitioning to stratified squamous epithelium at the external os.

o Vagina: muscular tube lined by stratified squamous epithelium that provides protection and lubrication.

The virtual library section of the female genital system showcases histological features essential for understanding both normal and pathological conditions. Common histopathological lesions include: endometrial hyperplasia, endometriosis, endometrial carcinoma, uterine leiomyosarcoma, cervical dysplasia, as precancerous cervical intraepithelial lesions or benign cellular changes, often linked to HPV infection, or ovarian benign or malignant tumors, with distinct histological patterns, some of them represented in our virtual slide collection, both histologically or cytologically.

Thus, this virtual histology collection of the female genital system not only illustrates the normal histological features of these structures but also provides insights into various pathological conditions. Understanding these histological aspects is crucial for diagnosis and management of female reproductive health issues.

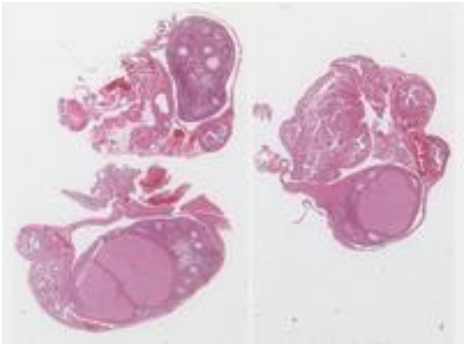
14.1 Ovary #1



The slide shows an ovary, lined by a simple cuboidal epithelium (germinal epithelium), supported by tunica albuginea (dense irregular connective tissue). The parenchyma is divided into cortex, the location of oocytes development, and the medulla. Ovarian follicles, composed of an oocyte surrounded by follicular cells display several types. Primordial follicles are located in the outer cortex and are each formed by an oocyte, surrounded by a single layer of flat follicular cells. Primary follicles contain a larger oocyte, surrounded by an eosinophilic glycoproteic layer (zona pellucida) and by a single layer of follicular cells (unilaminar primary follicle) or by more layers of cuboidal-shaped follicular or granulosa cells (multilaminar primary follicle). Secondary (antral) follicles contain an antrum (a fluid-filled space) and a larger oocyte, surrounded by a thicker zona pellucida, and by granulosa cells. These granulosa cells are distributed in corona radiata, with several layers immediately surrounding the oocyte, cumulus oophorus (proliger), forming a group of cells anchored to the follicle wall, and parietal granulosa (stratum granulosum), as several layers of cells that surround the antrum. Theca folliculi surrounds the external basal lamina of stratum granulosum, with stromal cells that develop into an inner cellular layer, rich in blood vessels (theca interna) and an outer fibrous layer (theca

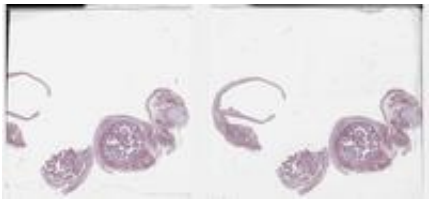
externa). Mature or Graafian follicles are the largest type, containing a larger antrum and a thinner stratum granulosum by comparison with the secondary follicles, transforming into luteal body, after ovulation. Its involution give rise to corpus albicans, while involution of all types of follicles lead to atretic follicles. Ovarian stroma is a highly cellular connective tissue with numerous spindle cells and fewer connective tissue fibers. Medulla is composed of fibro-elastic connective tissue with many large, tortuous blood vessels, lymph vessels, and nerve fibers.

14.2 Ovary #2



The slide shows an ovary, lined by a simple cuboidal epithelium (germinal epithelium), supported by tunica albuginea (dense irregular connective tissue). The parenchyma is divided into cortex, the location of oocytes development, and the medulla. Ovarian follicles, composed of an oocyte surrounded by follicular cells display several types. Primordial follicles are located in the outer cortex and are each formed by an oocyte, surrounded by a single layer of flat follicular cells. Primary follicles contain a larger oocyte, surrounded by an eosinophilic glycoproteic layer (zona pellucida) and by a single layer of follicular cells (unilaminar primary follicle) or by more layers of cuboidal-shaped follicular or granulosa cells (multilaminar primary follicle). Secondary (antral) follicles contain an antrum (a fluid-filled space) and a larger oocyte, surrounded by a thicker zona pellucida, and by granulosa cells. These granulosa cells are distributed in corona radiata, with several layers immediately surrounding the oocyte, cumulus oophorus (proliger), forming a group of cells anchored to the follicle wall, and parietal granulosa (stratum granulosum), as several layers of cells that surround the antrum. Theca folliculi surrounds the external basal lamina of stratum granulosum, with stromal cells that develop into an inner cellular layer, rich in blood vessels (theca interna) and an outer fibrous layer (theca externa). Mature or Graafian follicles are the largest type, containing a larger antrum and a thinner stratum granulosum by comparison with the secondary follicles, transforming into luteal body, after ovulation. Its involution give rise to corpus albicans, while involution of all types of follicles lead to atretic follicles. Ovarian stroma is a highly cellular connective tissue with numerous spindle cells and fewer connective tissue fibers. Medulla is composed of fibro-elastic connective tissue with many large, tortuous blood vessels, lymph vessels, and nerve fibers.

14.3 Fallopian Tube #1



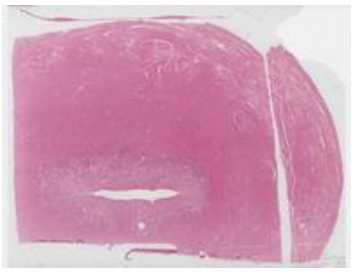
The slide shows an oviduct (Fallopian or uterine tube), with three layers. Mucosa has folds that project into the lumen, lined by simple columnar epithelium, with ciliated cells and

peg cells, supported by lamina propria, with blood vessels and nerves. Muscularis is comprised of an inner circular or spiral layer and an outer longitudinal layer. Serosa is composed of a simple flat epithelium (or mesothelium) supported by a thin layer of connective tissue.

14.4 Uterus - mid-late secretory endometrium

The slide shows a specimen of the uterus during the mid-late secretory phase. The uterine wall is composed of three layers: endometrium, as a specialized mucosa that undergoes marked changes during the menstrual or endometrial cycle, myometrium, and perimetrium. Endometrium is divided into functional layer (stratum functionalis), comprising the upper two thirds, supplied by spiral (coiled) arteries and basal layer, supplied by straight arteries. The surface is lined by simple columnar epithelium (lining epithelium and endometrial glands) and endometrial lamina propria (stroma). Surface epithelium invaginates into the stroma, forming convoluted, irregularly-shaped contour endometrial glands, with intraluminal eosinophilic secretions. The glands are lined by a simple low columnar to cuboidal epithelium. Stroma presents increased edema and pre-decidual changes. The basal layer (stratum basalis) occupies the lower third of the mucosa and is preserved during menstruation, regenerating the functional layer. Myometrium is composed of three indistinct layers of smooth muscle (inner and outer layers contain mostly longitudinal bundles of smooth muscle, while the middle layer (stratum vasculare) is the thickest layer of mostly circular or spiral or network bundles of smooth muscle with numerous blood vessels almost devoid of adventitia. Perimetrium is composed of a thin layer of connective tissue lined by an outer serous layer or visceral peritoneum.

14.5 Uterus - early secretory endometrium



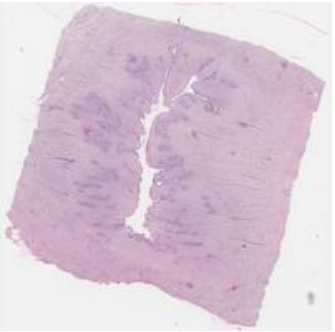
The slide shows a specimen of the uterus during the early secretory phase. The uterine wall is composed of three layers: endometrium, as a specialized mucosa that undergoes marked changes during the menstrual or endometrial cycle, myometrium, and perimetrium. Endometrium is divided into functional layer (stratum functionalis), comprising the upper two thirds, supplied by spiral (coiled) arteries and basal layer supplied by straight arteries. The surface is lined by a surface lining epithelium of simple columnar type forming endometrial glands and endometrial lamina propria (stroma). Slightly wavy, convoluted endometrial glands, with narrow lumens, and scarce secretion are seen. The glands are lined by a simple columnar epithelium with subnuclear vacuoles in > 50% of each gland. The basal layer (stratum basalis) occupies the lower third of the mucosa and is preserved during menstruation,

regenerating the functional layer. Myometrium is composed of three indistinct layers of smooth muscle (inner and outer layers contain mostly longitudinal bundles of smooth muscle, while the middle layer (stratum vasculare) is the thickest layer of mostly circular or spiral or network bundles of smooth muscle with numerous blood vessels almost devoid of adventitia. Perimetrium is composed of a thin layer of connective tissue lined by an outer serous layer or visceral peritoneum.

14.6 Uterus – proliferative endometrium #1

The slide shows a specimen of the uterus during the proliferative phase. The uterine wall is composed of three layers: endometrium, as a specialized mucosa that undergoes marked changes during the menstrual or endometrial cycle, myometrium, and perimetrium. Endometrium is divided into functional layer (stratum functionalis), comprising the upper two thirds, supplied by spiral (coiled) arteries and basal layer, supplied by straight arteries. Endometrium is lined by surface epithelium, a simple columnar epithelium forming both the lining epithelium and the endometrial glands, and endometrial lamina propria (stroma). Endometrial glands are formed by surface epithelium that invaginates into the stroma, with a straight or slightly wavy contour, narrow lumens, and scarce secretion. The basal layer (stratum basalis) occupies the lower third of the mucosa and is preserved during menstruation, regenerating the functional layer. Myometrium is composed of three indistinct layers of smooth muscle. Inner and outer layers contain mostly longitudinal bundles of smooth muscle, while the middle layer (stratum vasculare) is the thickest layer of mostly circular or spiral or network bundles of smooth muscle, with numerous blood vessels almost devoid of adventitia. Perimetrium is composed of a thin layer of connective tissue lined by an outer serous layer or visceral peritoneum.

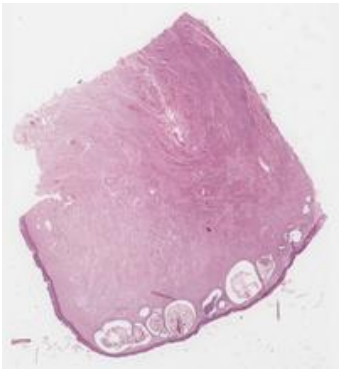
14.7 Uterine cervix #1



The slide shows the cervix, which is composed of mucosa and the cervical wall, comprised of dense connective tissue rich in both collagen and elastic fibers, with reduced smooth muscle. Endocervix forms the wall of the cervical canal, being lined by mucus-secreting simple columnar epithelium continuous with the lining of the body of the uterus and endocervical glands, branched glands with mucus-secreting cells located in the lamina propria. The surface epithelium focally presents immature squamous metaplasia. Ectocervix (exocervix) is protruding into the vagina (portio vaginalis) and contains the opening of the uterus (external os). It is lined by stratified squamous non-

keratinized epithelium, continuous with the lining of the vagina. The transformation zone represents the abrupt junction between the simple columnar endocervical epithelium and the exocervical squamous epithelium (not seen on this slide).

14.8 Uterine cervix #2

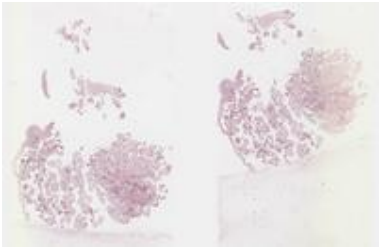


The slide shows the cervix, which is composed of mucosa and the cervical wall, comprised of dense connective tissue rich in both collagen and elastic fibers, with reduced smooth muscle. Endocervix forms the wall of the cervical canal, being lined by mucus-secreting simple columnar epithelium continuous with the lining of the body of the uterus and endocervical glands, branched glands with mucus-secreting cells located in the lamina propria. Ectocervix (exocervix) is protruding into the vagina (portio vaginalis) and contains the opening of the uterus (external os). It is lined by stratified squamous non-keratinized epithelium, continuous with the lining of the vagina. The squamo-columnar junction or the transformation zone represents the abrupt transition between the simple columnar endocervical epithelium and the exocervical squamous epithelium (not seen on this slide). Nabothian cysts are also seen, due to accumulation of mucus in obstructed endocervical glands.

14.9 Uterus - atrophic endometrium

The slide shows a cross section of uterus. The endometrium exhibits small endometrial glands lined by cuboidal or columnar epithelium without evidence of mitotic figures or hormonal effects, and scant strips of cuboidal epithelium with little or no underlying stroma (atrophic glands). Additionally, large hemorrhagic areas are seen. Vessels exhibiting arteriolosclerosis added with calcifications are frequently observed within myometrium.

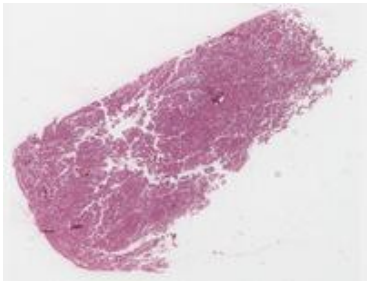
14.10 Placenta Ist semester



The slide shows a placenta of early pregnancy, composed of both fetal component and maternal component. Chorial (placental) villi, representing projections of the fetal chorion that extend into lacunae in which maternal blood flows, are seen in cross sections. The villi wall is lined by cuboidal epithelium consisting of cytotrophoblast, with cuboidal cells with pale staining cytoplasm and

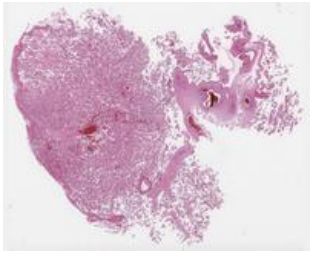
euchromatic nuclei and syncytiotrophoblast layer, with multinucleated cuboidal cells with microvilli. The core of the villi is composed of mesenchymal connective tissue, which contains numerous fetal capillaries and venules. Fragments of the maternal decidua basalis, containing decidual cells, as clusters of large round to oval cells can also be seen. There is also an acidophilic amorphous material associated with both components, named fibrinoid.

14.11 Placenta IInd semester #1



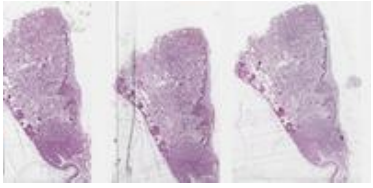
The slide shows a placenta of late pregnancy, composed of both fetal component and maternal component. Chorial (placental) villi, representing projections of the fetal chorion that extend into lacunae in which maternal blood flows, are seen in cross sections. The villi wall is lined by simple cuboidal epithelium, consisting only of syncytiotrophoblast layer, with multinucleated cuboidal cells with microvilli. The core of the villi is composed of mesenchymal connective tissue, which contains numerous fetal capillaries and venules. There are also fragments of the maternal decidua basalis, containing decidual cells, as clusters of large round to oval cells. There is also an acidophilic amorphous material associated with both components, named fibrinoid.

14.12 Placenta IInd semester #2



The slide shows a placenta of late pregnancy, composed of both fetal component and maternal component. Chorial (placental) villi, representing projections of the fetal chorion that extend into lacunae in which maternal blood flows, are seen in cross sections. The villi wall is lined by simple cuboidal epithelium consisting only of syncytiotrophoblast layer, with multinucleated cuboidal cells with microvilli. The core of the villi is composed of mesenchymal connective tissue, which contains numerous fetal capillaries and venules. There are also fragments of the maternal decidua basalis, containing decidual cells, as clusters of large round to oval cells. There is also an acidophilic amorphous material associated with both components, named fibrinoid.

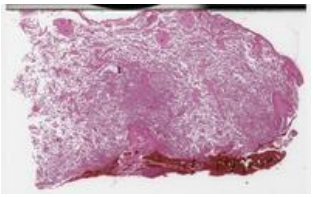
14.13 Placenta IInd semester #3



The slide shows a placenta of late pregnancy, composed of both fetal component and maternal component. Chorial (placental) villi, representing projections of the fetal chorion that extend into lacunae in which maternal blood flows, are seen in cross sections. The villi wall is lined by simple cuboidal epithelium, consisting only of

syncytiotrophoblast layer, with multinucleated cuboidal cells with microvilli. The core of the villi is composed of mesenchymal connective tissue, which contains numerous fetal capillaries and venules. There are also fragments of the maternal decidua basalis, containing decidual cells, as clusters of large round to oval cells. There is also an acidophilic amorphous material associated with both components, named fibrinoid.

14.14 Retroplacental hematoma

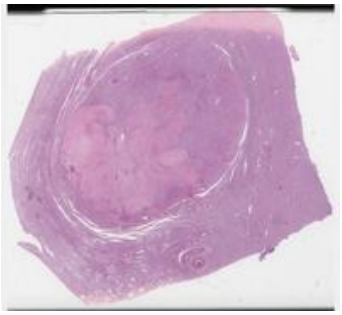


The slide shows decidual or retroplacental hemorrhage or hematoma, with focal extension into the placental parenchyma (intraparenchymal extension). There is minimal infarction of the placental parenchyma. Intravillous hemorrhages or villous stromal hemorrhages are also seen.

14.15 Uterine leiomyosarcoma #1

The slide shows a conventional or spindle cell type leiomyosarcoma with the following features: proliferation of myoid cells with marked cytologic atypia and ≥ 10 mitoses / 10 high power fields. Additionally, there may be tumor cell necrosis, with an abrupt transition from viable tumor cells to necrotic cells (ghost cells and apoptotic bodies). The growth pattern is characterized by long intersecting or haphazard fascicles, with typical infiltrative borders. The cytologic features are: spindle or elongated cells, with eosinophilic cytoplasm, hyperchromatic nuclei with moderate to severe nuclear pleomorphism, and atypical mitoses. Multinucleated and osteoclast-like giant cells may be sometimes noticed.

14.16 Uterine leiomyosarcoma #2



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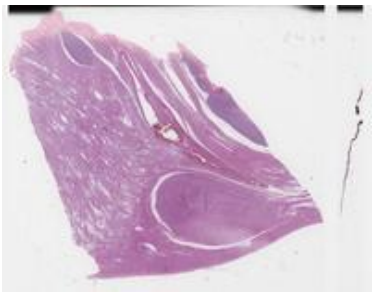
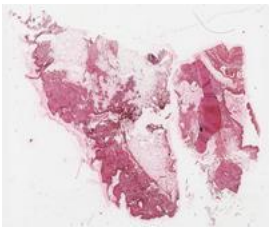
14.17 Uterine leiomyosarcoma #3



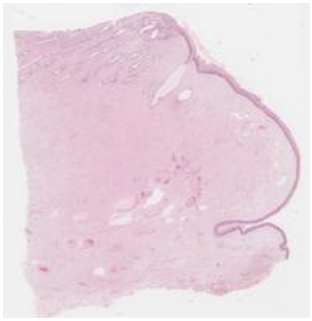
The slide shows a conventional or spindle cell type leiomyosarcoma with the following features: proliferation of myoid cells with marked cytologic atypia and ≥ 10 mitoses / 10 high power fields. Additionally, there may be tumor cell necrosis, with an abrupt transition from viable tumor cells to necrotic cells (ghost cells and apoptotic bodies). The growth pattern is characterized by long intersecting or haphazard fascicles, with typical infiltrative borders. The cytologic features are: spindle or elongated cells, with eosinophilic cytoplasm, hyperchromatic nuclei, with moderate to severe nuclear pleomorphism, and atypical mitoses. Multinucleated and osteoclast-like giant cells may be sometimes noticed.

14.18 Mature ovarian teratoma



The slide shows an ovarian mass characterized by the proliferation of numerous mature benign tissues originating from all three embryonic layers: ectodermal tissue, with focal salivary gland acini, mesodermal tissue, and endodermal tissue.

14.19 Cervix



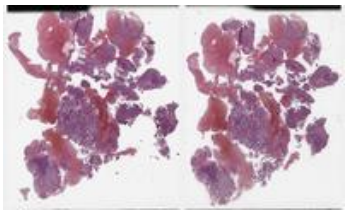
The slide shows the cervix, which is composed of mucosa and the cervical wall, with dense connective tissue rich in both dense collagen fibers and elastic fibers, with reduced smooth muscle. Endocervix forms the wall of the cervical canal, being lined by mucus-secreting simple columnar epithelium continuous with the lining of the body of the uterus and endocervical glands, branched glands with mucus-secreting cells located in the lamina propria. The transformation zone may be also seen, as the abrupt junction between the simple columnar endocervical epithelium and the exocervical squamous epithelium. Nabothian cysts may be also seen, due to accumulation of mucus in obstructed endocervical glands.

14.20 Uterus - proliferative endometrium #2

The slide shows a specimen of the uterus during the proliferative phase. The uterine wall is composed of three layers: endometrium, as a specialized mucosa that undergoes marked changes during the menstrual or endometrial cycle, myometrium, and perimetrium.

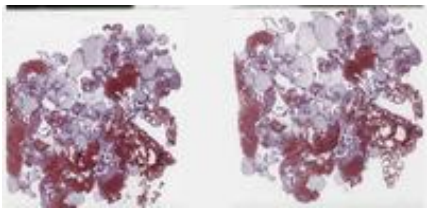
Endometrium is divided into functional layer (stratum functionalis), comprising the upper two thirds, supplied by spiral (coiled) arteries and basal layer (stratum basalis), supplied by straight arteries. The surface is lined by simple columnar epithelium (lining epithelium and endometrial glands) and endometrial lamina propria (stroma). Endometrial glands are formed by surface epithelium that invaginates into the stroma, with a straight or slightly wavy contour, narrow lumens, and scarce secretion. The basal layer (stratum basalis) occupies the lower third of the mucosa and is preserved during menstruation, regenerating the functional layer. Myometrium is composed of three indistinct layers of smooth muscle. The inner and outer layers contain mostly longitudinal bundles of smooth muscle. The middle layer - stratum vasculare is the thickest layer of mostly circular, spiral or network of bundles of smooth muscle with numerous blood vessels, almost devoid of adventitia. Perimetrium is composed of a thin layer of connective tissue lined by an outer serous layer or visceral peritoneum.

14.21 Endometrial clear cell carcinoma



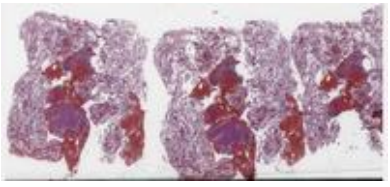
The slide shows a malignant proliferation of hobnail and flat cells, with an associated solid, glandular, and papillary architecture. The tumor cells have abundant clear or eosinophilic cytoplasm, pleomorphic nuclei, and moderate mitotic index. The associated stroma exhibits focal hyalinization.

14.22 Complete hydatiform mole



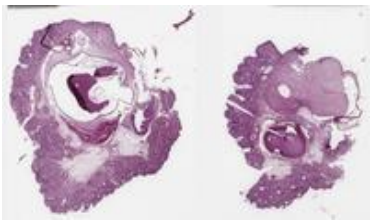
The slide shows chorionic villi with diffuse enlargement, marked hydropic changes, and cistern formation. The villi are lined by trophoblast with marked circumferential hyperplasia, cytologic atypia, and mitoses. A fragment of decidualized endometrium infiltrated by intermediate type trophoblast (exaggerated placental site) is also seen.

14.23 Early pregnancy loss - 11 weeks



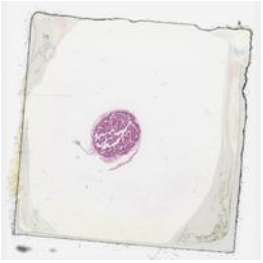
The slide shows irregularly shaped chorionic villi with stromal edema and myxoid degeneration. The villi are lined by a bilayered trophoblast (inner cytotrophoblast and outer syncytiotrophoblast). Fragments of decidualized endometrium can also be noted.

14.24 Mature ovarian cystic teratoma



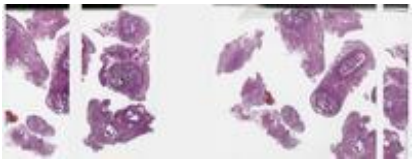
The slide shows an ovarian multilocular cystic structure characterized by the proliferation of numerous mature benign tissues originating from all three embryonic layers: ectoderm, mesoderm, and endoderm (thin epidermis with skin adnexa – sebaceous glands, hair follicles, apocrine sweat glands, as well as adipose tissue, smooth muscle fibers, tracheal tissues – pseudostratified epithelium, mucous secreting tubulo-acinar glands, hyaline cartilage plates, bone tissue, and adult tooth-like structures). The residual ovarian tissue contains a corpus luteum cyst and follicular cysts.

14.25 Fallopian tube #2



The slide shows a Fallopian tube (oviduct or uterine tube), in its ampullar region, with three layers. Mucosa has folds that project into the lumen, being lined by simple columnar epithelium, with ciliated cells and peg cells, and lamina propria, with blood vessels and nerves. Muscularis is comprised of an inner circular or spiral layer and an outer longitudinal layer. Serosa is composed of a simple flat epithelium (mesothelium) supported by a thin layer of connective tissue.

14.26 Salpingitis isthmica nodosa



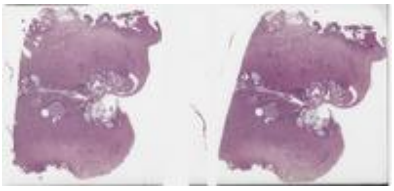
The slide shows discrete and dilated glandular lumina, unaccompanied by stroma and completely surrounded by smooth muscle. The gland-like structures are lined by a normal appearing ciliated tubal-type epithelium, with no cytologic atypia. There is no associated inflammatory response.

14.27 Vagina

The slide shows a fragment of vagina, a fibromuscular tube that connects the internal reproductive organs to the external environment. It is lined by mucosa with stratified squamous non-keratinized epithelium, rich in glycogen, associated with connective tissue papillae, rich in elastic fibers and leukocytes, originating from the underlying lamina propria that project into the epithelial layer, without glands. The deeper lamina propria is denser, with many thin-walled vessels and is analogous to a submucosa. In humans, keratohyalin granules may be present in

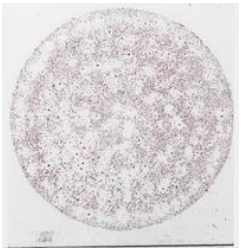
the epithelial cells, but under normal conditions, keratinization does not occur. A muscular layer is organized into two sometimes indistinct, intermingling smooth muscle layers, an outer longitudinal layer, and an inner circular layer. The outer layer is continuous with the corresponding layer in the uterus and is much thicker than the inner layer. Striated muscle fibers of the bulbospongiosus muscle are present at the vaginal opening. An outer adventitia is organized into an inner dense connective tissue layer adjacent to the muscularis, rich in elastic fibers, and an outer loose connective tissue layer, with numerous blood and lymphatic vessels and nerves, that blends with the adventitia of the surrounding structures. The greater and lesser vestibular glands located in the wall of the vaginal vestibule produce mucus that lubricates the vagina together with the cervical mucus. The vagina has few general sensory nerve endings, mainly in its lower third.

14.28 Uterine cervix - tunnel clusters and Nabothian cysts



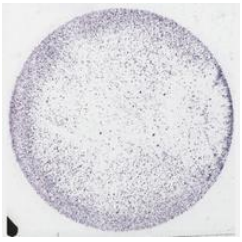
The slide shows a benign proliferation of endocervical glands with lobular configuration, with cystically dilated glands (type B tunnel clusters). Dilated mucin filled cysts (Nabothian cysts) lined by a simple cuboidal-columnar epithelium, with variable amounts of mucinous cytoplasm and round to oval nuclei without mitotic activity are associated with tunnel clusters.

14.29 L-SIL with HPV-related koilocytosis - liquid-based PAP smear



The slide shows a cytological preparation, containing cervical superficial, intermediate, parabasal, and basal squamous cells, along with few endocervical cells. Some intermediate cells have enlarged hyperchromatic nuclei with irregular borders and clear perinuclear halos, suggesting HPV cytopathic effect (koilocytes #1, #2).

14.30 Vaginosis - liquid-based PAP smear

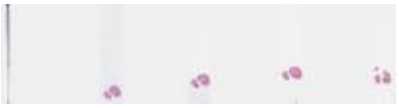


The liquid based PAP smear shows a relatively clean background, consisting of superficial and intermediate epithelial cells, endocervical cells arranged in patches and isolated, rare neutrophils, frequent coccobacilli sometimes adherent to the cells surface ("clue cells") - suggestive of a shift of the vaginal flora - bacterial vaginosis), and mucus.

14.31 Cervical adenocarcinoma associated with HPV - cervical biopsy

The slide shows fragments of cervical mucosa which present a stromal infiltration of irregularly shaped malignant confluent endocervical glands with focal cribriform architecture, without a lobular arrangement, within a desmoplastic stroma. The tumoral glands present a mucin depleted pseudostratified or stratified columnar epithelium, with elongated hyperchromatic nuclei, with coarse chromatin, and apical mitoses.

14.32 Condyloma - HPV-related

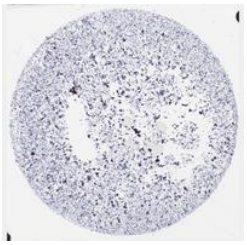


The slide shows a benign HPV-related lesion with warty appearance, lined by a stratified squamous epithelium with acanthosis, papillomatosis, hyperkeratosis, and hypergranulosis. The epithelial papillae are broad and present fused rounded ends. The epithelium contains rare keratinocytes with viral cytopathic effect (koilocytes).

14.33 Trichomonas vaginalis infection - liquid-based PAP smear

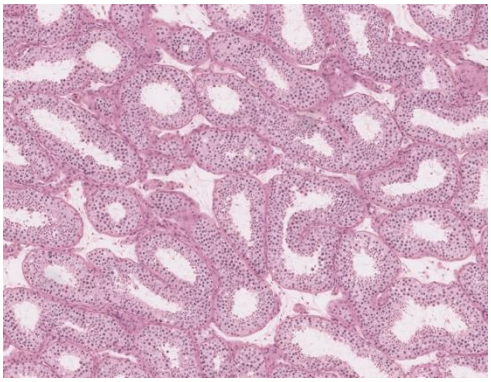
The liquid based PAP smear shows an inflammatory background, consisting of superficial and intermediate epithelial cells, most with obvious reactive changes associated with inflammation (slight nuclear hypertrophy with preservation of the nuclear-cytoplasmic ratio, with small perinuclear halo, polychromatophilia of the cytoplasm), endocervical cells, relatively frequent neutrophils, bacilli, rare pear-shaped microorganisms with eccentric, elongated nucleus, with intracytoplasmic eosinophilic granulations - compatible with Trichomonas vaginalis #1, #2.

14.34 L-SIL with koilocytosis



The liquid based PAP smear shows a relatively clean background, consisting of superficial and intermediate epithelial cells, endocervical cells being absent. Few cells show mature cytoplasm, intermediate and superficial, with koilocytic appearance (with minimal nuclear atypia - nuclear hypertrophy of approximate 3 times larger than the nucleus of a normal intermediate cell, obvious hyperchromasia, slightly irregular nuclear outline, change of the nuclear-cytoplasmic ratio in favour of the nucleus, evident perinuclear halo with peripheral condensation of the cytoplasm, suggestive of HPV cytopathic effect.

CHAPTER 15 - Male Reproductive System



The male genital system is responsible for reproduction and consists of both external and internal structures. From a histological perspective, this system is made up of various tissues specialized for the production, storage, and transport of sperm, as well as the secretion of male sex hormones, primarily testosterone. The main components include the testes, epididymis, vas deferens, seminal vesicles, prostate gland, and penis.

The testes are the primary male reproductive organs, where spermatogenesis and testosterone production occur. Histologically, the testes are composed of seminiferous tubules, lined by Sertoli cells that support and nourish developing sperm cells, and germ cells in various stages of spermatogenesis. Leydig cells, located in the interstitial tissue between the tubules, are responsible for testosterone synthesis. The process of spermatogenesis is tightly regulated by hormones from both the pituitary gland and the testes, ensuring the continuous production of sperm.

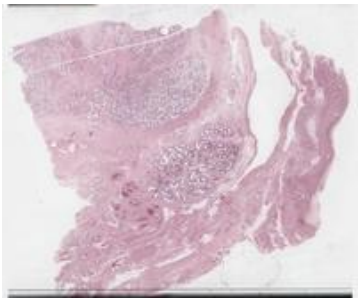
Once sperm are formed, they are transported to the epididymis, a long coiled duct where they mature and gain motility. The epididymis is lined by pseudostratified columnar epithelium with stereocilia, which aid in sperm maturation and storage. From the epididymis, sperm travel through the *vas deferens* , a muscular tube lined by a similar epithelium, where they are stored until ejaculation.

Accessory glands, including the seminal vesicles and prostate gland, play a vital role in producing the seminal fluid that nourishes and protects sperm. The seminal vesicles secrete a fructose-rich fluid that provides energy for sperm, while the prostate contributes by enzymes and other products that enhance sperm motility and longevity. Histologically, the prostate is made up of glandular tissue surrounded by fibromuscular stroma, with secretory cells that produce the prostatic fluid, as a significant portion of semen.

The penis, composed of erectile tissue, plays a central role in the delivery of sperm during intercourse. It contains three cylindrical masses of erectile tissue - two corpora cavernosa and one corpus spongiosum - surrounded by dense connective tissue, called tunica albuginea. The erectile tissue is richly vascularized, allowing it to become engorged with blood during erection.

The male genital system is susceptible to various pathologies, many of which affect fertility and sexual function. Common conditions include benign prostatic hyperplasia (BPH), which involves non-cancerous enlargement of the prostate, often leading to urinary symptoms. Prostate cancer is another significant pathology, being one of the most common cancers in men. Testicular cancer, although less common, primarily affects younger males and typically arises from the germ cells within the seminiferous tubules. Other conditions, such as erectile dysfunction and infertility, can arise from hormonal imbalances, vascular issues, or damage to the reproductive organs.

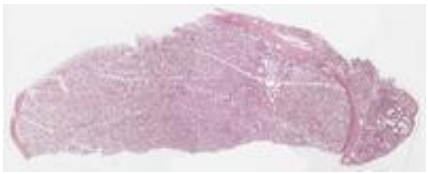
15.1 Testis #1



The slide is a section of testis, covered by a capsule, with its inner surface named tunica vasculosa, as a thin, loose connective tissue layer that contains blood vessels. The mediastinum projects into the testis, containing blood and lymphatic vessels, rete testis, and the proximal portions of the efferent ductules. Incomplete connective tissue septa that project from the mediastinum toward the capsule divide each testis into approximately 250 lobules. Each lobule contains 1-4 highly coiled seminiferous tubules, of 30-80 cm in length and 150-250 µm in diameter, forming loops that end in short straight tubules, named tubuli recti. The seminiferous tubules are lined with a complex stratified epithelium, the seminiferous epithelium (male germinal epithelium). There are two distinct cell population in the epithelium: spermatogenic and supporting cells. Spermatogenic cells are the male germ cells that replicate and migrate from the basal lamina to the lumen, as they mature. They consist of several cell types. Spermatogonia are adjacent to the basal lamina and are several types: type Ad (dark ovoid nucleus), as stem cells, type Ap (pale ovoid nucleus), which undergoes differentiation, and type B (spherical nucleus with chromatin clumps), which undergoes mitotic divisions. Primary spermatocytes (big nucleus with visible chromatin threads) and secondary spermatocytes (smaller nucleus with dense chromatin) are the next type, which undergo meiotic divisions to form secondary spermatocytes, which form spermatids. Spermatids (early, with small round dense nuceus and late, with very small spindle-shaped dark dense nucleus and no visible cytoplasm) reside in the apical portion of the epithelium. They mature into the sperm (spermatozoa) by spermiogenesis. Additionally, supporting Sertoli (sustentacular) cells are the true epithelial cells of the seminiferous tubules. Each Sertoli cell extends through the full thickness of the seminiferous epithelium. They are columnar cells with complex basal, lateral, and apical domains that surround the developing spermatogenic cells and exhibit a pale ovoid or triangular nucleus, with euchromatin. Peritubular tissue is formed of multilayer connective tissue which closely surrounds each of the

seminiferous tubules. The tunica propria consists of typical basal lamina, a collagenous layer, 3-5 layers of myoid cells (peritubular contractile cells, with characteristics of both fibroblasts and smooth muscle cells), blood and lymphatic vessels. The loose connective tissue between the seminiferous tubules contains interstitial endocrine cells (Leydig cells), blood and lymphatic vessels, nerves, fibroblasts, macrophages and mast cells. Active Leydig cells in testosteron secretion are large, irregularly polygonal, acidophilic cells that are often filled with lipid droplets. Abundant smooth endoplasmic reticulum (sER), mitochondria with tubulovesicular cristae, as well as rod-shaped cytoplasmic crystals (of Reinke) are their characteristics.

15.2 Testis #2



The slide is a section of testis, covered by a capsule, with its inner surface named tunica vasculosa, as a thin, loose connective tissue layer that contains blood vessels. The mediastinum projects into the testis, containing blood and lymphatic vessels, rete testis, and the proximal portions of the efferent ductules. Incomplete connective tissue septa that project from the mediastinum toward the capsule divide each testis into approximately 250 lobules. Each lobule contains 1-4 highly coiled seminiferous tubules, of 30-80 cm in length and 150-250 µm in diameter, forming loops that end in short straight tubules, named tubuli recti. The seminiferous tubules are lined with a complex stratified epithelium, the seminiferous epithelium (male germinal epithelium). There are two distinct cell population in the epithelium: spermatogenic and supporting cells. Spermatogenic cells are the male germ cells that replicate and migrate from the basal lamina to the lumen, as they mature. They consist of several cell types. Spermatogonia are adjacent to the basal lamina and are several types: type Ad (dark ovoid nucleus), as stem cells, type Ap (pale ovoid nucleus), which undergoes differentiation, and type B (spherical nucleus with chromatin clumps), which undergoes mitotic divisions. Primary spermatocytes (big nucleus with visible chromatin threads) and secondary spermatocytes (smaller nucleus with dense chromatin) are the next type, which undergo meiotic divisions to form secondary spermatocytes, which form spermatids. Spermatids (early, with small round dense nuceus and late, with very small spindle-shaped dark dense nucleus and no visible cytoplasm) reside in the apical portion of the epithelium. They mature into the sperm (spermatozoa) by spermiogenesis. Additionally, supporting Sertoli (sustentacular) cells are the true epithelial cells of the seminiferous tubules. Each Sertoli cell extends through the full thickness of the seminiferous epithelium. They are columnar cells with complex basal, lateral, and apical domains that surround the developing spermatogenic cells and exhibit a pale ovoid or triangular nucleus, with euchromatin. Peritubular tissue is formed of multilayer connective tissue which closely surrounds each of the seminiferous tubules. The tunica propria consists of typical basal lamina, a collagenous layer, 3-5 layers of myoid cells (peritubular contractile cells, with characteristics of both fibroblasts and smooth muscle cells), blood and lymphatic vessels. The loose connective tissue between the seminiferous tubules contains interstitial endocrine cells (Leydig cells), blood and lymphatic

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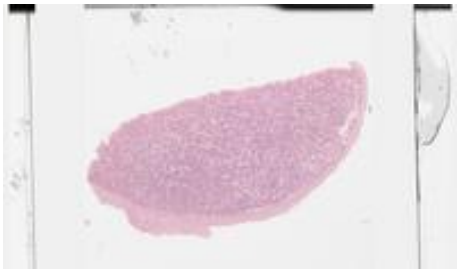
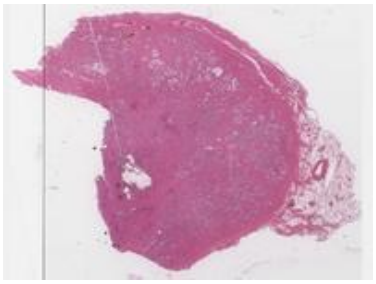
15.3 Testis #3



The slide is a section of testis, covered by a capsule, with its inner surface named tunica vasculosa, as a thin, loose connective tissue layer that contains blood vessels. The mediastinum projects into the testis, containing blood and lymphatic vessels, rete testis, and the proximal portions of the efferent ductules. Incomplete connective tissue septa that project from the mediastinum toward the capsule divide each testis into approximately 250 lobules. Each lobule contains 1-4 highly coiled seminiferous tubules, of 30-80 cm in length and 150-250 µm in diameter, forming loops that end in short straight tubules, named tubuli recti. The seminiferous tubules tubules are lined with a complex stratified epithelium, the seminiferous epithelium (male germinal epithelium). There are two distinct cell population in the epithelium: spermatogenic and supporting cells. Spermatogenic cells are the male germ cells that replicate and migrate from the basal lamina to the lumen, as they mature. They consist of several cell types. Spermatogonia are adjacent to the basal lamina and are several types: type Ad (dark ovoid nucleus), as stem cells, type Ap (pale ovoid nucleus), which undergoes differentiation, and type B (spherical nucleus with chromatin clumps), which undergoes mitotic divisions. Primary spermatocytes (big nucleus with visible chromatin threads) and secondary spermatocytes (smaller nucleus with dense chromatin) are the next type, which undergo meiotic divisions to form secondary spermatocytes, which form spermatids. Spermatids (early, with small round dense nuceus and late, with very small spindle-shaped dark dense nucleus and no visible cytoplasm) reside in the apical portion of the epithelium. They mature into the sperm (spermatozoa) by spermiogenesis. Additionally, supporting Sertoli (sustentacular) cells are the true epithelial cells of the seminiferous tubules. Each Sertoli cell extends through the full thickness of the seminiferous epithelium. They are columnar cells with complex basal, lateral, and apical domains that surround the developing spermatogenic cells and exhibit a pale ovoid or triangular nucleus, with euchromatin. Peritubular tissue is formed of multilayer connective tissue which closely surrounds each of the seminiferous tubules. The tunica propria consists of typical basal lamina, a collagenous layer, 3-5 layers of myoid cells (peritubular contractile cells, with characteristics of both fibroblasts and smooth muscle cells), blood and lymphatic vessels. The loose connective tissue between the seminiferous tubules contains interstitial endocrine cells (Leydig cells), blood and lymphatic vessels, nerves, fibroblasts, macrophages and mast cells. Active Leydig cells in testosteron secretion are large, irregularly polygonal, acidophilic cells that are often filled with lipid droplets. Abundant smooth endoplasmic reticulum (sER),

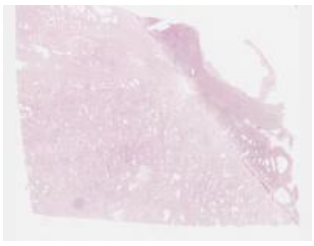
mitochondria with tubulovesicular cristae, as well as rod-shaped cytoplasmic crystals (of Reinke) are their characteristics.

15.4 Prostate #1



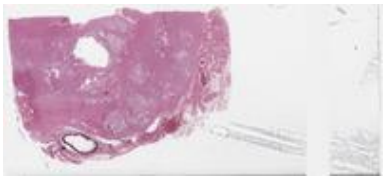
The slide shows a collection of 30 to 50 tubuloalveolar glands arranged in concentric layers that surround the proximal urethra, forming the prostate. The mucosal layer contains short glands that secrete directly into the urethra, followed by a submucosal layer of glands, and an outer layer of main glands. Both submucosal and main glands have ducts that carry their secretions to the prostatic urethra. Simple columnar epithelium generally lines the glandular structures of the prostate, although patches of cuboidal, squamous or pseudostratified epithelium may be observed. The prostatic alveoli, especially those in older men, usually contain concretions of variable form and size, called corpora amylacea. The stroma of prostate gland is formed by mixed fibromuscular tissue.

15.5 Benign prostatic hyperplasia #1



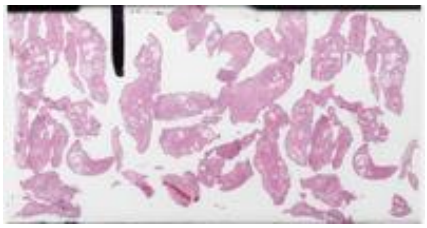
The slide shows a relatively nodular lesion made up of variably sized glandular structures, which are lined by secretory and basal cells. There a frequent glandular dilatation with papillary infoldings and some small cysts. The epithelial lining is ranging from low cuboidal to columnar, with pink pale cytoplasm, regular, rounded, centrally located nuclei and generally inconspicuous nucleoli. Stromal tissue, rich in smooth muscle fibers, contains focal leukocytes.

15.6 Prostate carcinoma



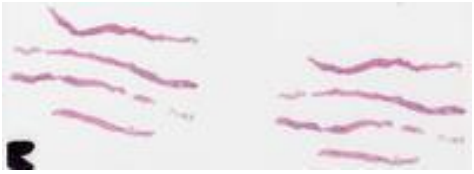
The slide shows an infiltrative growth of glands or poorly cohesive single cells, lined by atypical cells with nuclear enlargement, nucleolar prominence, some with amphophilic cytoplasms, with lack of basal layer. Focal cribriform pattern is noticed. There are also mitoses and apoptotic bodies. Intraluminal contents focally exhibit crystalloids, with pink amorphous secretions. There is added adipose tissue invasion, vascular invasion, along with stromal desmoplasia.

15.7 Benign prostatic hyperplasia #2



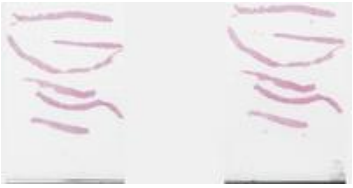
The slide contains prostate tissue fragments removed by TUR-P (transurethral resection of the prostate) showing benign prostatic hyperplasia. There is epithelial nodular hyperplasia, formed by variably sized glandular structures, which are lined by both secretory and basal cells, with focal glandular dilatation, along with papillary infoldings, often containing corpora amylacea. Epithelial lining is variable, from flat to columnar, with pale pink cytoplasm, centrally located nuclei, with inconspicuous nucleoli. There may be also some stromal nodules, which consists of bland spindle cells, with round-ovoid nuclei. There is added cystic atrophy and and chronic inflammation (chronic prostatitis).

15.8 Non-specific granulomatous prostatitis



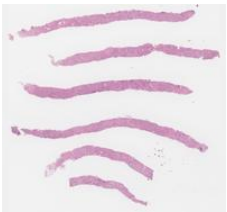
The slide contains prostate tissue fragments removed by prostate biopsy, showing multiple foci of chronic granulomatous inflammation, with epitheliod cells and multinucleated cells. There is also visible glandular tissue, with focal metaplastic changes.

15.9 Prostatic adenocarcinoma moderately differentiated - biopsy



The slide contains prostate tissue fragments removed by prostate biopsy, showing small tumor glands with preserved lumina (grade Gleason 3) along with distorted tumor glands with no outlined lumen and areas with cribriform architecture (Gleason grade 4). Perineural invasion can be seen. Summing the grades, Gleason Score 7 (3+4) results, with a prognostic grade group 3.

15.10 Prostatic adenocarcinoma - biopsy



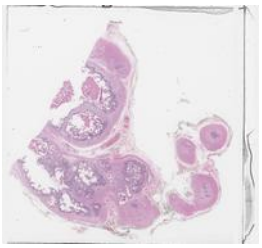
The slide contains prostate tissue fragments removed by prostate biopsy, showing distorted tumor glands with no outlined lumen and areas with cribriform architecture (Gleason grade 4) and poorly cohesive tumor cells sometimes arranged in strings (Gleason grade 5). Summing the grades, Gleason Score 9 (4+5) results, with a prognostic grade group 5.

15.11 Prostate #2

The slide shows a collection of 30 to 50 tubuloalveolar glands arranged in concentric layers that surround the proximal urethra, forming the prostate. The mucosal layer contains short glands that secrete directly into the urethra, followed by a submucosal layer of glands, and an outer layer of main glands. Both submucosal and main glands have ducts that carry their secretions to the prostatic urethra. Simple columnar epithelium generally lines the glandular structures of the prostate, although patches of cuboidal, squamous or pseudostratified epithelium may be observed. The prostatic alveoli, especially those in older men, usually contain concretions of variable form and size, called corpora amylacea. The stroma of prostate gland is formed by mixed fibromuscular tissue.

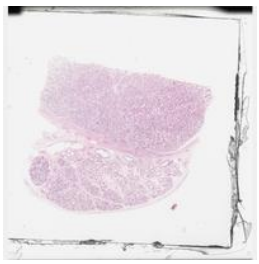
15.12 Seminal vesicles

The slide contains fragments of the seminal vesicles, which are paired, elongated, folded tubular glands, with muscular and fibrous coats. The glandular structures are lined by pseudostratified columnar epithelium, which contains tall noncilliated cells and short round cells that rest on the basal lamina. Columnar cells are protein-secreting cells (well developed rough endoplasmic reticulum - rER and large secretory vacuoles in the apical cytoplasm). Mucosa forms primary, secondary and tertiary folds to increase the surface area for secretion. The presence of amorphic acidophilic secretion in the lumen of seminal vesicles is a characteristic feature.

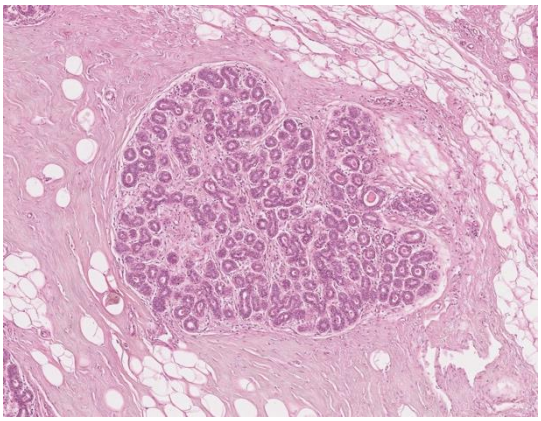


15.13 Testis and excurrent duct system

The slide shows a fragment of testis along with excurrent duct system. Approximately 15 efferent ductules (ductuli efferentes) leave the testis by penetrating the tunica albuginea and connect rete testis to the proximal portion of the ductus epididymis. They are lined with alternating clumps of tall and short columnar cells, thus giving rise to the saw-toothed appearance of the luminal surface. Tall columnar cells are generally ciliated and are believed to have a role in sperm movement. The short nonciliated cells have numerous microvilli and canalicular invaginations of the apical domain. The muscular coat consists of few to several layers of myocytes. Ductus epididymis is approximately 6 m long, as a highly coiled tube in which sperm undergo further maturation. Ductus epididymis is divided into head (caput), a body (corpus) and a tail (cauda). Efferent ductules empty into epididymis head. The body and tail of ductus epididymis is lined with a pseudostratified epithelium, consisting of tall columnar principal cells and short basal cells. Principal cells vary from 40 to 80 µm tall. Apical domain is characterized by the presence of long, modified microvilli (named stereocilia), of 10 to 25 µm in length. There are abundant lymphocytes visible between basal cells, called halo cells. A thin muscle layer covers the epididymis head and most of its body. Additional thick layers (inner and outer) are added in epididymis tail.



CHAPTER 16 - Mammary glands



The mammary glands are specialized exocrine organs responsible for lactation, providing essential nutrients to infants. Histologically, they consist of lobules and ducts, which are embedded in adipose and fibrous connective tissue, and they undergo significant changes throughout a woman's life due to hormonal influences.

The mammary glands can be divided into the following components:

· Lobules: functional units where milk is produced, composed of glandular epithelial cells surrounded by myoepithelial cells that facilitate milk ejection.

· Ducts: tubular structures that transport milk from the lobules to the nipple, lined with a specialized epithelium that varies in structure and function depending on hormonal status.

The histological composition of the mammary gland includes various cell types and structures:

· Glandular epithelium: composed of cuboidal to columnar epithelial cells responsible for milk synthesis; these cells exhibit cytoplasmic features indicative of secretory activity, including well-developed endoplasmic reticulum and Golgi apparatus.

· Myoepithelial cells: located between the basement membrane and the epithelial cells, these contractile cells play a crucial role in facilitating milk flow.

· Adipose tissue: provides structural support and plays a role in hormone metabolism, influencing the function and development of the mammary glands.

Functionally, the mammary glands play several vital roles in: (i) lactogenesis, the process of milk production, stimulated by hormonal changes during pregnancy and postpartum, and (ii) milk ejection reflex, process mediated by oxytocin, which triggers contraction of myoepithelial cells to expel milk during breastfeeding.

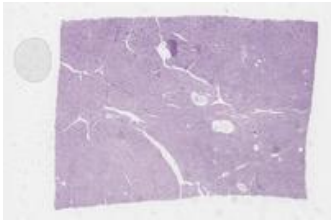
The mammary gland undergoes cyclic changes during the menstrual cycle, pregnancy, and lactation. Hormones, such as estrogen, progesterone, and prolactin, induce these changes, leading to proliferation of the glandular epithelium, also influencing the surrounding stroma.

The mammary gland can be affected by various conditions, such as: (i) fibrocystic changes, which are common benign alterations characterized by cyst formation and stromal fibrosis, (ii) mastitis, inflammation of the mammary tissue, often due to infection, which can lead to abscess formation, or (iii) ductal carcinoma in situ (DCIS) and invasive carcinomas, which represent neoplastic conditions that can arise from the ductal or lobular epithelium, often characterized by distinct histopathological features that aid in diagnosis.

This virtual library section showcases the histological characteristics of normal and pathological mammary gland tissues, serving as a foundational resource for understanding the histopathological features associated with benign and malignant lesions, such as breast carcinoma, atypical hyperplasia, and other conditions that impact mammary gland health. The slides illustrate the intricate relationship between the histology of the mammary glands and the physiological processes they govern, highlighting their role in both health and disease.

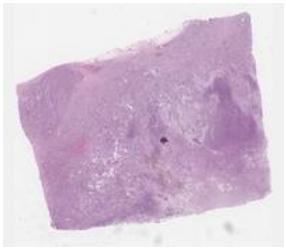
16.1 Breast fibroadenoma #1

The slide shows a circumscribed, encapsulated breast tumor, containing a biphasic pattern of growth (glandular and stromal). Glandular component has two recognized growth patterns: intracanalicular, with linear branching structures delimited by proliferating stroma and pericanalicular, with open lumens separated by expanded stroma. Glandular elements have an intact myoepithelial cell layer.

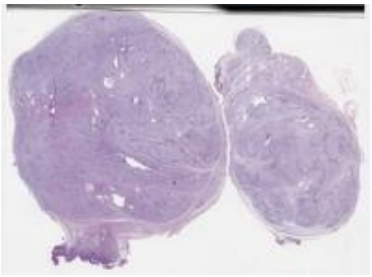


16.2 Breast ductal carcinoma

The slide shows breast fibro-adipose tissue containing infiltrative solid nests, cords or individual tumor cells with moderately enlarged nuclei, with conspicuous nucleoli, eosinophilic cytoplasm, and variable mitoses, that compress the prominent desmoplastic stroma. A focus of ductal carcinoma in situ (DCIS) is observed.

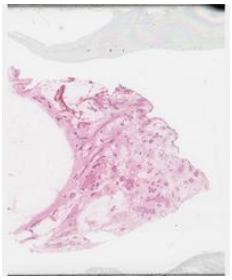


16.3 Breast fibroadenoma #2



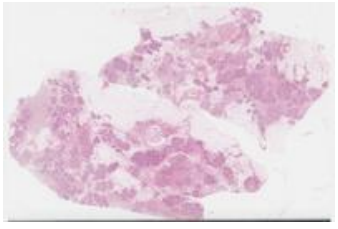
The slide shows a circumscribed, encapsulated breast tumor, containing a biphasic pattern of growth (glandular and stromal). Glandular component has two recognized growth patterns: intracanalicular (predominant): linear branching structures delimitated by proliferating stroma and pericanalicular: open lumens separated by expanded stroma. Glandular elements have an intact myoepithelial cell layer.

16.4 Mammary gland #1



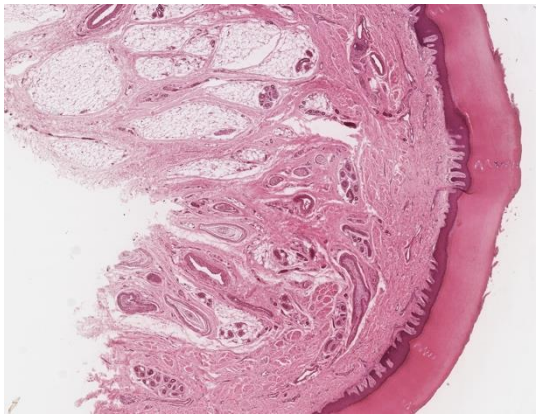
The slide shows mammary gland, as a compound, tubulo-alveolar gland. Resting (inactive) mammary gland is composed of 15 to 20 lobes separated by septa of connective tissue with adipose cells. Each lobe is drained by a single lactiferous duct that opens into the nipple, lined by a double layer of cuboidal or columnar cells surrounded by a sheath of connective tissue with myoid cells. Lobules are enclosed by a thin layer of connective tissue. Intralobular ducts are lined by one layer of cuboidal cells surrounded by myoepithelial cells and a thin layer of connective tissue. During pregnancy, terminal ductules differentiate into secretory alveoli, lined by simple cuboidal to columnar epithelium, with secretory cells that synthesize and secrete milk, rich in proteins, lipids, and lactulose, with large secretion granules. Intralobular stroma is composed of loose connective tissue with few adipose cells.

16.5 Mammary gland #2



The slide shows mammary gland, as a compound, tubulo-alveolar gland. Resting (inactive) mammary gland is composed of 15 to 20 lobes separated by septa of connective tissue with adipose cells. Each lobe is drained by a single lactiferous duct that opens into the nipple, lined by a double layer of cuboidal or columnar cells surrounded by a sheath of connective tissue with myoid cells. Lobules are enclosed by a thin layer of connective tissue. Intralobular ducts are lined by one layer of cuboidal cells surrounded by myoepithelial cells and a thin layer of connective tissue. During pregnancy, terminal ductules differentiate into secretory alveoli, lined by simple cuboidal to columnar epithelium, with secretory cells that synthesize and secrete milk, rich in proteins, lipids, and lactulose, with large secretion granules. Intralobular stroma is composed of loose connective tissue with few adipose cells.

CHAPTER 17 - Integumentary System



The integumentary system is the largest organ of the body that forms a physical barrier between the external and the internal environment. The integumentary system includes the epidermis, dermis, hypodermis, associated glands, hair, and nails. The integumentary system has many different functions, such as thermoregulation, protection, added to metabolic and sensory roles. The hypodermis is also called the subcutaneous connective tissue, which stores adipose tissue, being recognized as the superficial fascia of gross anatomy.

Epidermis has the following five layers:

The stratum germinativum provides the germinal cells necessary for the regeneration of the layers of the epidermis, being composed of germinal cells, separated by a thin basement membrane from the underlying dermis. After a mitotic division a newly formed cells will undergo a progressive maturation, called keratinization, as they migrate to the surface.

The stratum spinosum contains the cells originating in the statum germinativum and display desmosomes on their outer surface.

The stratum granulosum contains cells which accumulate dense basophilic keratohyalin granules.

The stratum lucidum is only seen in thick epidermis and represents a transition from the stratum granulosum to stratum corneum, containing cells that are filled with eleidin.

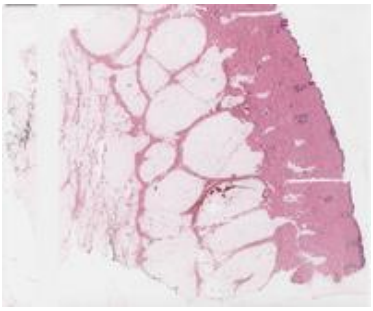
The stratum corneum may retain their desmosomal junctions in the deep layers, but as they are pushed to the surface by newly forming cells of the stratum germinativum, the dead cells gradually break apart and are lost, a process called desquamation.

The dermis is typically subdivided into two zones, a papillary dermis and a reticular layer. The dermis contains mostly fibroblasts which are responsible for collagen, elastin, and ground substance secretion, providing the support and elasticity of the skin. The dermis also contains

immune cells that are involved in defence against foreign invaders. The reticular layer of the dermis consists of dense irregular connective tissue, which differs from the papillary layer which is made up of loose connective tissue.

The integumentary system contains a variety of appendages, as hair follicles, sweat glands, and sebaceous glands. The hair root sheath is composed of external and internal layers. The external root sheath represents an extension of epidermis, while the internal root sheath is composed of three layers, Henle's layer, Huxley's layer, and an internal cuticle that is continuous with the outermost layer of the hair shaft.

17.1 Skin - thin epidermis #1

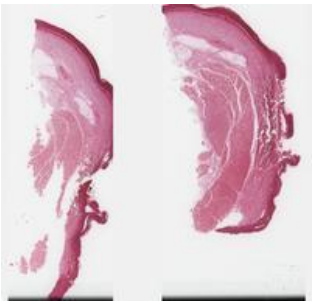


The so-called “thin skin”, based on the thickness of epidermis, has around 1-2 mm, covering most of the body, being composed of thin epidermis, dermis, and supported by hypodermis. The surface epithelium is thin epidermis (keratinized stratified squamous epithelium), composed of the following four layers: stratum basale (basal layer), made up of a single layer of germinal regenerative cells resting on the basement membrane, which is attached to the superficial dermis, stratum spinosum, made up of polygonal keratinocytes attached to each other by desmosomes or spiny processes, discontinuous stratum granulosum (granular layer), made up of keratinocytes with numerous basophilic granules in their cytoplasm, and stratum corneum (cornosum layer), as a thin layer of dead cells devoid of nuclei and organelles. Dermis is a connective tissue that supports the epidermis, composed of dermal papillae, with loose connective tissue, rich in capillaries and reticular (deep) dermis, made up of dense irregular connective tissue, containing skin adnexa. The skin adnexa are: eccrine sweat glands, as coiled tubular glands, with lightly stained secretory portions and darkly stained ducts, lined by bistratified cuboidal epithelium, sebaceous glands, and hair follicles.

17.2 Skin with thin epidermis electrical burn marks

The slide shows thermoelectric damage of the skin lined by thin epidermis. There is focal nuclear streaming or palisading of the epidermis, added to steam blisters situated in the epidermis, at the dermal-epidermal junction, or in dermis.

17.3 Skin with thick epidermis electrical burn marks

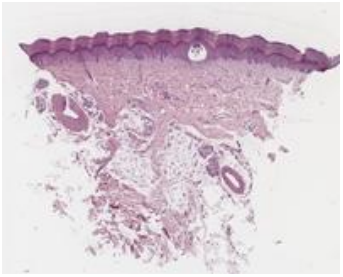


The slide shows thermoelectric damage of the skin lined by thick epidermis. The fragment also contains hypodermis and subjacent striated muscle. There is focal dissolution of the epidermis and superficial dermis, associated with variable hemorrhage and a brown-blackish material covering the denuded surfaces. Focal nuclear streaming or palisading of the epidermis, added to hemorrhagic steam blisters situated mainly at the dermal-epidermal junction are also seen.

17.4 Skin epidermal cyst

The slide shows a skin fragment containing a cyst lined by stratified squamous epithelium, including a granular layer. The cyst wall does not contain eccrine sweat glands, sebaceous glands or hair follicles. The content of the cyst is represented by abundant keratin flakes. A foreign body giant cell reaction is present in the surrounding tissue due to rupture of the cyst.

17.5 Skin - thick epidermis #1



The skin is the largest human organ and has a variety of functions, including mechanical protection and sensory function. This slide presents a fragment of so-called "thick skin", based on the epidermis thickness, which is mainly found on the palms of the hands and the soles of the feet. Skin epithelium is a keratinized stratified squamous epithelium that consists of five layers: the stratum germinativum, stratum spinosum, stratum granulosum, stratum lucidum, which is difficult to see, and stratum corneum, from basal to apical location. The basal layer is composed of cuboidal stem cells with high mitotic activity. These cells migrate towards the surface, forming the different layers of the epidermis, until they reach the last layer formed mainly by keratin. The "thick skin" has a wide stratum corneum and the subjacent dermis is devoid of hair follicles and sebaceous glands. The slide also shows eccrine sweat glands.

17.6 Cutaneous cryptococcosis - skin biopsy, Giemsa staining

The slide contains a cutaneous fragment with epidermis showing discrete spongiosis and elongated epithelial ridges. The dermis shows nodules composed of vascular connective tissue with marked edema and a minimal amount of congestion. The vascular lumina and perivascular

spaces contain numerous round yeasts of variable size with round, slightly basophilic nuclei. These are surrounded by a characteristic pale, clear halo. Morphological features specific to Cryptococcus neoformans (round hyphae of variable size) are seen in Giemsa staining.

17.7 Cutaneous cryptococcosis - skin biopsy, H&E staining

The slide contains a cutaneous fragment with epidermis showing discrete spongiosis and elongated epithelial ridges. The dermis shows nodules composed of vascular connective tissue with marked oedema and a minimal amount of congestion. The vascular lumina and perivascular spaces contain numerous round yeasts of variable size with round, slightly basophilic nuclei. These are surrounded by a characteristic pale, clear halo. Morphological features specific to Cryptococcus neoformans (round hyphae of variable size with an intense eosinophilic gelatinous halo) may be seen in PAS and Giemsa stainings.

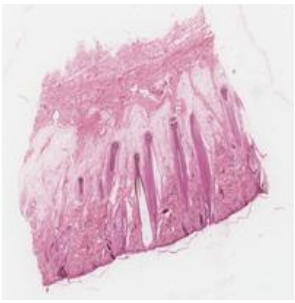
17.8 Cutaneous cryptococcosis - skin biopsy, PAS staining

The slide contains a cutaneous fragment with epidermis showing discrete spongiosis and elongated epithelial ridges. The dermis shows nodules composed of vascular connective tissue with marked oedema and a minimal amount of congestion. The vascular lumina and perivascular spaces contain numerous round yeasts of variable size with round, slightly basophilic nuclei. These are surrounded by a characteristic pale, clear halo. Morphological features specific to Cryptococcus neoformans (round hyphae of variable size with an intense eosinophilic gelatinous halo) are seen in PAS staining.

17.9 Skin - thick epidermis #2

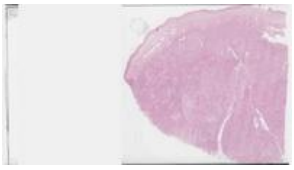
The skin is the largest human organ and has a variety of functions, including mechanical protection and sensory function. In this slide, we have an image of the so-called "thick skin", based on the epidermis thickness, which is mainly found on the palms of the hands and the soles of the feet. Skin epithelium is a keratinized stratified squamous epithelium that consists of five layers: the stratum germinativum, stratum spinosum, stratum granulosum, stratum lucidum, which is difficult to see, and stratum corneum, from basal to apical location. The basal layer is composed of cuboidal stem cells with high mitotic activity. These cells migrate towards the surface, forming the different layers of the epidermis, until they reach the last layer formed by keratin. The "thick skin" has a wide stratum corneum of epidermis and hair follicles and sebaceous glands are absent in dermis.

17.10 Skin - thin epidermis #2



The haired skin is composed of thin epidermis, dermis, and supported by hypodermis. The surface epithelium is thin epidermis (keratinized stratified squamous epithelium), composed of the following four layers: stratum basale (basal layer), made up of a single layer of germinal regenerative cells resting on the basement membrane, which is attached to the superficial dermis, stratum spinosum, made up of polygonal keratinocytes attached to each other by desmosomes or spiny processes, stratum granulosum (granular layer), made up of keratinocytes with numerous basophilic granules in their cytoplasm, and stratum corneum (cornosum layer), as a thin layer of dead cells devoid of nuclei and organelles. Dermis is a connective tissue that supports the epidermis, composed of dermal papillae, with loose connective tissue, rich in capillaries and reticular (deep) dermis, made up of dense irregular connective tissue, containing skin adnexa. The skin adnexa are: eccrine sweat glands, as coiled tubular glands, with lightly stained secretory portions and darkly stained ducts, lined by bistratified cuboidal epithelium, sebaceous glands, and hair follicles.

17.11 Cutaneous squamous cell carcinoma, NOS #1

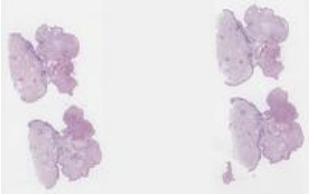


The slide exhibits a skin fragment containing large areas of carcinoma with atypical keratinocytes that infiltrate the dermis. The tumor shows a well differentiated grade given by easily recognizable squamous epithelium, with abundant keratinization, apparent intercellular bridges, minimal pleomorphism, and basal mitotic figures.

17.12 Cutaneous squamous cell carcinoma, NOS #2

The slide exhibits a skin fragment containing large areas of carcinoma with atypical keratinocytes that infiltrate the dermis. The tumor shows a moderately differentiated grade given by easily recognizable squamous epithelium, with reduced keratinization, apparent intercellular bridges, moderate pleomorphism, and mitotic figures. There is added tumor necrosis and abundant peritumoral lymphocytic inflammatory infiltrate.

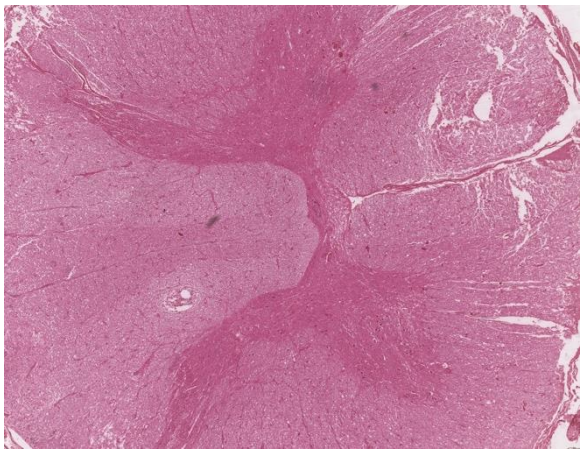
17.13 Cutaneous capillary hemangioma



The slide shows a skin fragment that contains a dermal benign tumor with a lobular appearance, consisting of small, closely packed capillaries, lined by a single layer of flattened endothelial cells with no features suggestive of malignancy.

CHAPTER 18 - Nervous System

From an anatomical point of view, the nervous system is organised into: central nervous system (CNS), which comprises the brain and spinal cord, which float in the cerebrospinal fluid (CSF) and peripheral nervous system (PNS), represented by cranial, spinal, peripheral nerves, and ganglia.



CNS is protected by a bony housing represented by the skull and vertebral column, associated with meninges, a triple-layered connective tissue sheath. The meninges includes dura mater, arachnoid, and pia mater.

The most significant regions of the CNS are the cerebrum, cerebellum, and spinal cord. CNS also displays white matter and grey matter areas, with different histological features caused by the specific distribution of neuronal bodies within grey matter.

Grey matter contains numerous neuronal cell bodies, the initial unmyelinated portions of axons, dendrites, along with astrocytes and microglial cells. Grey matter forms the cerebrum and the cerebellum cortex, and the deeper area of the spinal cord. The deep regions of the CNS contain aggregates consisting of abundant neuronal cell bodies, called nuclei.

The cerebral cortex contains neuronal cell bodies, dendrites, axons, and central glial cells, being the synapses location. Nuclei represent islands of gray matter, which are situated in the deep portions of the cerebrum and cerebellum. White matter contains only axons, some associated glial cells, and frequent blood vessels. The axons are functionally grouped into bundles, which are called tracts. The meshwork composed of dendritic, axonal, and glial processes, located in the gray matter, forms the neuropil.

Apart from cerebral cortex, the brain stem has not a precise delimitation into regions of white and gray matter, but is composed of islands surrounded by tracts of white matter.

The spinal cord may be described as a flattened cylindrical structure, which is in continuity with the brain stem. It exhibits an inner butterfly-shaped substance, with a grayish-tan appearance around the central canal, represented by the gray matter, surrounded by an external whitish

substance or the white matter, in cross-section. The motor neurons cell bodies that innervate striated muscle are large basophilic cells, situated in the grey matter of the ventral (anterior) horn.

Ependymal cells form the epithelium-like lining of CNS cavities. Within the system of the brain ventricles, this epithelium-like lining is further modified to produce CSF. The modified ependymal cells and the associated capillaries form the choroid plexus, which may sometimes display dystrophic calcifications.

The histopathology of CNS may be organized according to the etiology into traumatic, infectious or inflammatory, cerebrovascular, developmental, degenerative, neoplastic, traumatic, and toxic-metabolic. Meningitis is the inflammation of the meninges, which may be diagnosed in the onset of infectious or autoimmune inflammatory diseases. Infarction of CNS parenchyma is a common finding, due to thrombosis of an atherosclerotic artery, or to local vasospasm, or changes of blood pressure, or coagulopathy. Brain hemorrhages may have many potential causes and different locations in meninges or in parenchyma, many of cases being related to the hypertensive disease. Among the neoplastic pathology, meningiomas are relatively frequent tumors of the meninges and exhibit different histological types, according to the main cell type and their biological behavior. Different types of brain benign and malignant tumors may be diagnosed but brain tissue may also represent a host for different metastases, sometimes having a similar histological pattern with the primary tumors.

18.1 Brain tissue #1

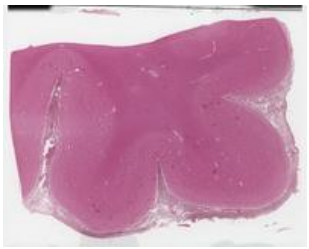
The slide consists of brain tissue, which comprises grey matter and white matter. Grey matter is composed of larger, triangular neuron cell bodies against the background of glial cells and neuropil. At higher magnification, neurons typically have large, pale nuclei with prominent nucleoli. The glial cells in the grey matter include oligodendrocytes (hyperchromatic, round nuclei, and abundant clear-appearing cytoplasm), astrocytes (paler, more elongated nuclei, and scant cytoplasm), and microglial cells. White matter is comprised mainly of myelinated axons and oligodendrocytes; the latter are responsible for myelination of the axons in the central nervous system.

18.2 Pons (brainstem)

Bundles of longitudinal fibres and transverse fibres are located ventrally in the basal pons, while the dorsal tegmentum forms part of the reticular formation. Bundles of longitudinal nerve fibres traverse the basal pons, interspersed by grey matter. Numerous cell bodies of

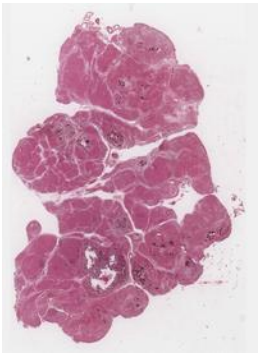
neurons and glial cells are seen in this region. The fourth ventricle is located dorsal to the tegmental pons. A layer of ependymal cells can be seen lining the cavity.

18.3 Pyogenic meningitis (purulent meningitis)



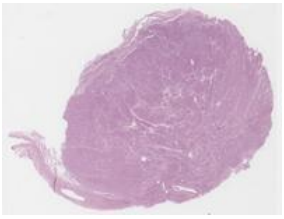
The slide shows a neutrophilic exudate involving the leptomeninges. There are also prominent dilated vessels. The leptomeninges also displays edema and abundant inflammation (extending down via the Virchow-Robin spaces) in the cortex. This type of acute or pyogenic meningitis is typical for bacterial infection.

18.4 Psammomatous meningioma



The slide shows a primary central nervous system tumor, arising from the arachnoid cap cells associated with dura mater, growing along the external surface of spinal cord or brain, Grade 1 variant. It shows a psammomatous pattern, with abundant psammoma bodies, and some intervening meningothelial cells.

18.5 Transitional meningioma



The slide shows a primary central nervous system tumor, arising from the arachnoid cap cells associated with dura mater, growing along external surface of the brain, Grade 1 variant. It shows a transitional type or mixed meningothelial and fibroblastic features. There are prominent whorls, psammoma bodies, and clusters of syncytial cells, added to fibroblastic spindle cells and thick collagen bundles.

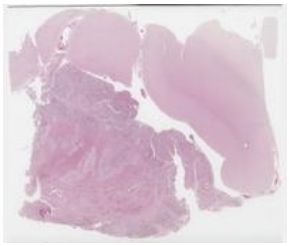
18.6 Cerebral ischemic infarction

The slide shows an ischemic chronic lesion (15 days - years). There are cavitated lesions, with vessels and macrophages surrounded by a glial scar, reactive astrocytes at the edge of the cavitation, with typical scattered hemosiderin laden macrophages (siderophages), focal hemorrhages, axonal balloons, and occasional perykaryal mineralization, with basophilia.

18.7 Cerebellum infarct - hemorrhagic stroke

The slide shows subacute infarction changes (5 - 14 days), characterized by macrophage infiltration and siderophages, variable neutrophilic infiltration, peripheral reactive astrocytosis and microglial activation (i.e., rod shaped microglia). Laminar necrosis occurs due to variable susceptibility to hypoxia among the cortex histological layers, with the most vulnerable neurons being Purkinje cells in the middle layer of the cerebellum. There is also neovascularization of necrotic tissue, along with reactive endothelial cells. Added chronic lesions (15 days - years), with cavitated pattern may be also seen.

18.8 Cerebral metastases

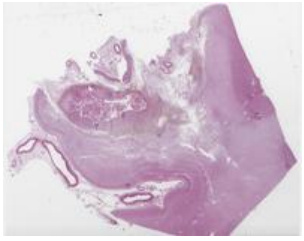


The slide shows large areas of malignant cells replacing the brain parenchyma, associated with tumor necrosis, added to infiltration of leptomeningeal tissue, and leptomeninges vascular tumor emboli. The remnant cerebral parenchyma shows vascular congestion along with focal microhemorrhages.

18.9 Subarachnoid hemorrhage

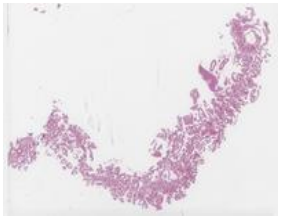
The slide shows brain tissue exhibiting areas of hemorrhage of the leptomeninges. The cerebral parenchyma contains congested blood vessels, without areas of hemorrhage.

18.10 Cerebral infarction stroke



The slide shows arteriolosclerosis associated with subacute infarction changes (5 - 14 days), characterized by macrophage infiltration and siderophages, variable neutrophilic infiltration, peripheral reactive astrocytosis and microglial activation (i.e., rod shaped microglia). There are hypereosinophilic neurons in the gray matter, neovascularization of necrotic tissue, along with reactive endothelial cells. There are added chronic lesions (15 days - years), with cavitated pattern, containing vessels and macrophages surrounded by a glial scar, reactive astrocytes at the cavitation edge, and hemosiderin laden macrophages.

18.11 Dystrophic calcifications of choroid plexus

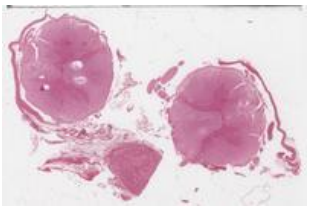


The slide shows projections or folds within the cavities of the central nervous tissue filled with cerebrospinal fluid. These folds, named choroid plexus, are lined by epithelium-like cells (ependymal cells), situated on a stromal connective tissue. They are cuboidal-columnar cells, without a basal lamina, tightly bound by apical junctional complexes, disposed on a single layer and are fluid-transporting cells. They also have basal infoldings, apical microvilli, and cilia. Basophilic areas of dystrophic calcification are randomly seen within these folds.

18.12 Brain tissue #2

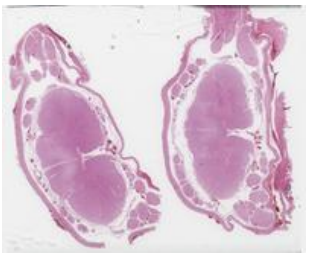
The slide consists of brain tissue, which comprises grey matter and white matter, covered by leptomeninges. Grey matter is composed of larger, triangular neuron cell bodies against the background of glial cells and neuropil. At higher magnification, neurons typically have large, pale nuclei with prominent nucleoli. The glial cells in the grey matter include oligodendrocytes (hyperchromatic, round nuclei and abundant clear-appearing cytoplasm), astrocytes (paler, more elongated nuclei, and scant cytoplasm), and microglial cells. White matter is comprised mainly of myelinated axons and oligodendrocytes; the latter are responsible for myelination of the axons in the central nervous system.

18.13 Spinal cord



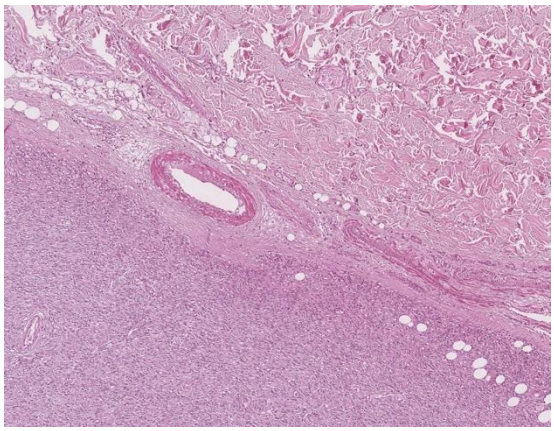
On a cross section, spinal cord is composed of centrally placed grey matter in form of a ventral horn and a dorsal horn, peripherally surrounded by the ventral, lateral and dorsal columns of white matter The ventral horns are prominent, with cell bodies of star-shaped motor neurons that supply the upper and lower extremities. Centrally, the central canal of the spinal cord, lined by ependymal cells, enables continuous cerebrospinal fluid flow from the ventricles of the brain. The columns of white matter are composed of cross sections of axons and their myelin sheaths.

18.14 Spinal cord #2



On a cross section, spinal cord is composed of centrally placed grey matter with butterfly-shaped ventral horns and dorsal horns, peripherally surrounded by the ventral, lateral, and dorsal columns of white matter, and covered by meninges. The ventral horns are prominent, with cell bodies of star-shaped motor neurons that supply the upper and lower extremities. Centrally, the central canal of the spinal cord (spinal foramen or ependymal canal), lined by ependymal cells, enables continuous cerebrospinal fluid flow from the ventricles of the brain. The columns of white matter are composed of cross sections of axons and their myelin sheaths.

CHAPTER 19 - Miscellaneous Histology, Histopathology & Cytology



Based on a systematic organization into sections, according to the tissues and systems of the body, added to a section dedicated for the training of young pathologists and nephrologists, the virtual library aims to introduce the undergraduate and postgraduate student into the world of microscopy.

However, yet another section allows the addition of virtual slides which did not fit into one of the body systems categories.

Currently, some virtual slides have been included in this section, either belonging to other histopathology domain beside those directly corresponding to histology counterparts, either to infectious histopathology, or either to toxic histopathology.

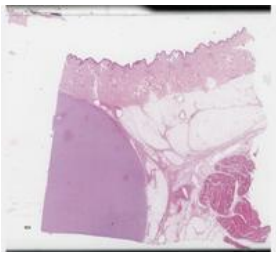
In the spectrum of mesenchymal neoplasms, those with fibroblastic differentiation may belong to dermatofibrosarcoma protuberans category, as one of the most common sarcomas involving the skin or subcutaneous tissue.

As a manifestation of ethylene glycol toxicity, detection of calcium oxalate crystals in the kidney may be easily done in hematoxylin-eosin (H&E) staining and certified in polarized light examination.

In the category of infectious disorders, one of the most common is candidiasis, with *Candida albicans* infection involving the skin or the mucous membranes, such as oral candidiasis characterized by budding yeasts and pseudohyphae. Another infectious disorder is caused by *Zygomycetes* fungi, including *Mucor* type, mostly related with immunocompromised patient, major trauma or invasive procedures, characterized by broad, sparsely septate or aseptate, thin-walled hyphae.

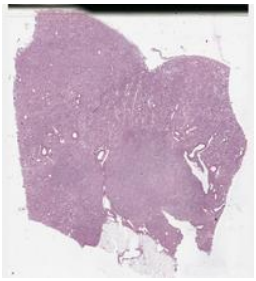
Other slides may be added in future in this section, which remains open for supplementation with other specimens, such as histology slides related to embryogenesis or histogenesis, slides related to the histopathological spectrum of soft tissue tumors, slides related to different accidental pathologies corresponding to toxic substances or other medico-legal circumstances, along with different types of cytology samples, either normal, infectious, suspicious for malignancy or clearly malignant.

19.1 Dermatofibrosarcoma



The slide shows a tumor centered within the dermis and subcutis, characterized by spindle cells with a storiform to whorled pattern, disposed in a collagenous stroma. The cytoplasm is generally abundant and eosinophilic. Nuclei are monomorphic and ovoid to elongated with variable mitotic activity. The tumor exhibits fat tissue infiltration, with typically spared adnexal structures.

19.2 Acute ethylene glycol poisoning (kidney)



The slide shows the presence of translucent polyhedral, rhomboid, and fan-like calcium oxalate crystals found within cortical and medullary tubular lumens. Crystals are birefringent under polarized light. There is also acute tubular injury. The background shows capsular and interstitial fibrosis, arteriolosclerosis, glomerulosclerosis, and focal chronic inflammatory infiltrate, corresponding to benign nephrosclerosis.

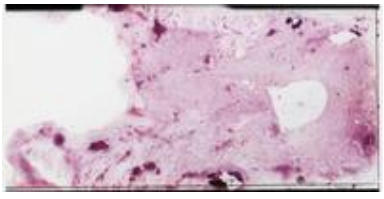
19.3 Oral pseudomembranous candidiasis (oral thrush) – mucosal biopsy, H&E staining #1

Fragments of oral mucosa with a necrotic appearance, composed of areas of stratified non-keratinized squamous epithelium, thick keratinized flaps and pseudomembranes containing candida hyphae and numerous round or round-oval spores specific to the genus Candidaalbicans.

19.4 Oral pseudomembranous candidiasis (oral thrush) – mucosal biopsy, H&E staining #2

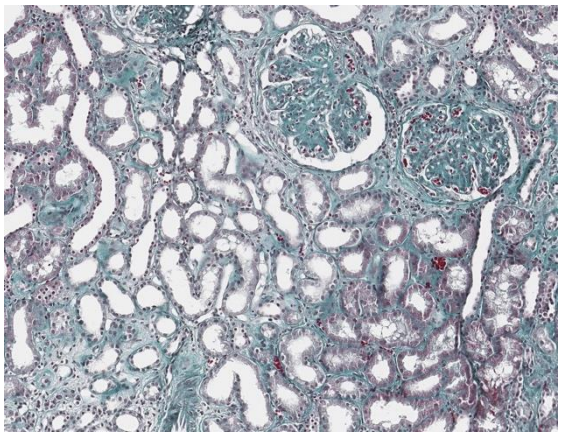
Fragments of oral mucosa with a necrotic appearance, composed of areas of stratified non-keratinized squamous epithelium, thick keratinized flaps and pseudomembranes containing candida hyphae and numerous round or round-oval spores specific to the genus Candida albicans.

19.5 Mucormycosis - lateral ventricle cerebrospinal fluid



This cytological preparation of the cerebrospinal fluid shows a polymorphic inflammatory cellular background (lymphocytes, histiocytes, and PMNs), with the presence of septate hyphae, an appearance suggestive of Mucormycosis.

CHAPTER 20 - Training pathologists' collection



This section is dedicated to difficult diagnoses, such as that of glomerulonephritis, but it is designed for future extension to other pathologies, which may be used for training and multidisciplinary team meetings.

Glomerulonephritis refers to a group of diseases characterized by inflammation of the glomeruli, the small filtration units within the kidney. These conditions can lead to impaired kidney function and, if left untreated, progress to chronic kidney disease or renal failure. Glomerulonephritis may arise due to primary kidney diseases or as a consequence of systemic diseases like lupus or vasculitis, where immune complex deposition or other immune-mediated processes injure the glomeruli.

From an etiological standpoint, glomerulonephritis can be classified into: primary glomerulonephritis, where the disease is confined to the kidneys, such as IgA nephropathy and minimal change disease and secondary glomerulonephritis, associated with systemic conditions like systemic lupus erythematosus (SLE), diabetes mellitus, or post-infectious glomerulonephritis.

Functionally, glomerulonephritis is distinguished by its effects on kidney function, including: nephritic syndrome and nephrotic syndrome.

This disorder results from immune system malfunctions, often involving the glomerular deposition of immune complexes, complement activation, and subsequent inflammation. Antibodies may directly target components of the glomerular basement membrane. The inflammation leads to the glomerular membranes thickening, endothelial or mesangial cells proliferation, and inflammatory cells infiltration, reducing the filtration capacity of the glomeruli.

Microscopically, glomerulonephritis displays various patterns of glomerular damage, ranging from mesangial expansion and segmental sclerosis to crescent formation. This histopathological diversity reflects the underlying immune processes involved and helps guide diagnosis and treatment. Common histological techniques used to study glomerulonephritis include light

microscopy, immunofluorescence to detect immune deposits, and electron microscopy to visualize ultrastructural changes in the glomerular basement membrane.

The clinical manifestations of glomerulonephritis are diverse, depending on the specific type and extent of glomerular injury. Patients may present with hematuria, proteinuria, reduced glomerular filtration rate (GFR), and, in severe cases, kidney failure. Diagnosis typically involves clinical evaluation, serologic testing, urinalysis, and kidney biopsy. Treatment is highly variable and depends on the cause of the disease, ranging from immunosuppressive therapy to address autoimmune components to supportive measures for managing hypertension and proteinuria.

Residency training emphasizes kidney biopsies opportunity, along with histological findings interpretation. Not only training pathologists but also training nephrologists need to understand the complex pathophysiology of glomerular injury, by collaboration with specialists like immunologists and pathologists, in multidisciplinary teams. Early intervention and personalized treatment can prevent disease progression to chronic kidney disease and renal failure, making this training crucial not only for young pathologists, but also for future nephrologists.

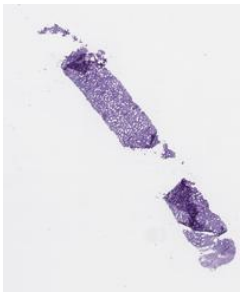
20.1 Membranoproliferative glomerulonephritis type 2_#1

The slide shows renal corpuscles with enlarged size, widened glomerular tufts, endocapillary hypercellularity, increased mesangial matrix and cellularity, homogeneously thickened basement membranes, prominent lobulation. Manifesting cellular or circumferential fibro-cellular crescents is also noticed. Interstitially, there is evident of chronic inflammation, fibrosis, and tubular atrophy.

20.2 Membranoproliferative glomerulonephritis type 2_#2

The slide shows renal corpuscles exhibiting enlarged size, with widened glomerular tufts, characterized by endocapillary hypercellularity, augmented mesangial matrix and mesangial cellularity, homogeneously thickened basement membranes, prominent lobulation, and focal glomerular collapse with incipient glomerular sclerosis. Additionally, renal corpuscles manifest the onset of cellular crescent.

20.3 Membranoproliferative glomerulonephritis type 2 - PAS staining



The slide shows renal corpuscles exhibiting enlarged size, with widened glomerular tufts, characterized by endocapillary hypercellularity, augmented mesangial matrix and mesangial cellularity, homogeneously thickened basement membranes, prominent lobulation, and focal glomerular collapse with incipient glomerular sclerosis. Additionally, renal corpuscles manifest the onset of cellular crescent.

20.4 Membranoproliferative glomerulonephritis type 2 - Masson's trichrome staining

The slide shows renal corpuscles exhibiting enlarged size, with widened glomerular tufts, characterized by endocapillary hypercellularity, augmented mesangial matrix and mesangial cellularity, homogeneously thickened basement membranes, prominent lobulation, and focal glomerular collapse with incipient glomerular sclerosis. Additionally, renal corpuscles manifest the onset of cellular crescent.

20.5 Membranoproliferative glomerulonephritis type 2 - Szekely trichrome staining

The slide shows renal corpuscles exhibiting enlarged size, with widened glomerular tufts, characterized by endocapillary hypercellularity, augmented mesangial matrix and mesangial cellularity, homogeneously thickened basement membranes, prominent lobulation, and focal glomerular collapse with incipient glomerular sclerosis. Additionally, renal corpuscles manifest the onset of cellular crescent.

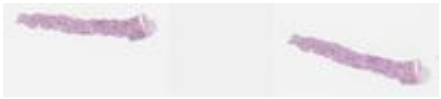
20.6 Membranoproliferative glomerulonephritis type 2 - Congo red staining

The slide shows renal corpuscles exhibiting enlarged size, with widened glomerular tufts, characterized by endocapillary hypercellularity, augmented mesangial matrix and mesangial cellularity, homogeneously thickened basement membranes, prominent lobulation, and focal glomerular collapse with incipient glomerular sclerosis. Additionally, renal corpuscles manifest the onset of cellular crescent.

20.7 Rapidly progressive glomerulonephritis_#1

The slide shows renal corpuscles exhibiting diverse characteristics: medium-sized corpuscles with thickened Bowman's capsule, rudimentary or absent glomeruli, or intact glomerular tufts. Additionally, signs of cellular crescents or fibro-cellular proliferation, marked endocapillary hypercellularity, thickened basement membranes, and moderate mesangial matrix expansion without hypercellularity are observed. Interstitially, there is marked chronic inflammation, either diffuse or compact, with accompanying fibrosis and tubular atrophy.

20.8 Rapidly progressive glomerulonephritis_#2



The slide shows renal corpuscles exhibiting diverse characteristics: medium-sized corpuscles with thickened Bowman's capsule, rudimentary or absent glomeruli, or intact glomerular tufts. Additionally, signs of cellular crescents or fibro-cellular proliferation, marked endocapillary hypercellularity, thickened basement membranes, and moderate mesangial matrix expansion without hypercellularity are observed. Interstitially, there is marked chronic inflammation, either diffuse or compact, with accompanying fibrosis and tubular atrophy.

20.9 Rapidly progressive glomerulonephritis- PAS staining

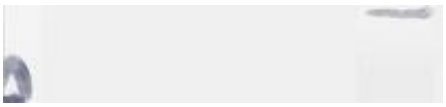
The slide shows renal corpuscles exhibiting diverse characteristics: medium-sized corpuscles with thickened Bowman's capsule, rudimentary or absent glomeruli, or intact glomerular tufts. Additionally, signs of cellular crescents or fibro-cellular proliferation, marked endocapillary hypercellularity, thickened basement membranes, and moderate mesangial matrix expansion without hypercellularity are observed. Interstitially, there is marked chronic inflammation, either diffuse or compact, with accompanying fibrosis and tubular atrophy.

20.10 Rapidly progressive glomerulonephritis- Masson's trichrome staining

The slide shows renal corpuscles exhibiting diverse characteristics: medium-sized corpuscles with thickened Bowman's capsule, rudimentary or absent glomeruli, or intact glomerular tufts. Additionally, signs of cellular or fibro-cellular crescent, marked endocapillary hypercellularity, thickened basement membranes, and moderate mesangial matrix expansion

without hypercellularity are observed. Interstitially, there is marked chronic inflammation, either diffuse or compact, with accompanying fibrosis and tubular atrophy.

20.11 Rapidly progressive glomerulonephritis - Szekely trichrome staining



The slide shows renal corpuscles exhibiting diverse characteristics: medium-sized corpuscles with thickened Bowman's capsule, rudimentary or absent glomeruli, or intact glomerular tufts. Additionally, signs of cellular crescents or fibro-cellular proliferation, marked endocapillary hypercellularity, thickened basement membranes, and moderate mesangial matrix expansion without hypercellularity are observed. Interstitially, there is marked chronic inflammation, either diffuse or compact, with accompanying fibrosis and tubular atrophy.

20.12 Rapidly progressive glomerulonephritis - Congo red staining

The slide shows renal corpuscles exhibiting diverse characteristics: medium-sized corpuscles with thickened Bowman's capsule, rudimentary or absent glomeruli, or intact glomerular tufts. Additionally, signs of cellular crescents or fibro-cellular proliferation, marked endocapillary hypercellularity, thickened basement membranes, and moderate mesangial matrix expansion without hypercellularity are observed. Interstitially, there is marked chronic inflammation, either diffuse or compact, with accompanying fibrosis and tubular atrophy.

20.13 Focal segmental glomerulosclerosis

The slide shows renal corpuscles with heterogeneous aspects: some are completely sclerosed, while others show an apparently intact glomerular tuft. Some demonstrate slight hypercellularity of endothelial cells, while others exhibit mesangial hypercellularity accompanied by increased mesangial matrix. This involvement typically affects a couple to three glomerular lobules, leading to subsequent collapse and features indicative of lobular sclerosis. Additionally, a prominent chronic inflammatory interstitial infiltrate and interstitial fibrosis are observed.

20.14 Focal segmental glomerulosclerosis - PAS staining

The slide shows renal corpuscles with heterogeneous aspects: some are completely sclerosed, while others show an apparently intact glomerular tuft. Some demonstrate slight hypercellularity of endothelial cells, while others exhibit mesangial hypercellularity accompanied by increased mesangial matrix. This involvement typically affects a couple to three glomerular lobules, leading to subsequent collapse and features indicative of lobular sclerosis. Additionally, a prominent chronic inflammatory interstitial infiltrate and interstitial fibrosis are observed.

20.15 Focal segmental glomerulosclerosis - Masson's trichrome staining

The slide shows renal corpuscles with heterogeneous aspects: some are completely sclerosed, while others show an apparently intact glomerular tuft. Some demonstrate slight hypercellularity of endothelial cells, while others exhibit mesangial hypercellularity accompanied by increased mesangial matrix. This involvement typically affects a couple to three glomerular lobules, leading to subsequent collapse and features indicative of lobular sclerosis. Additionally, a prominent chronic inflammatory interstitial infiltrate and interstitial fibrosis are observed.

20.16 Focal segmental glomerulosclerosis - Szekely trichrome staining

The slide shows renal corpuscles with heterogeneous aspects: some are completely sclerosed, while others show an apparently intact glomerular tuft. Some demonstrate slight hypercellularity of endothelial cells, while others exhibit mesangial hypercellularity accompanied by increased mesangial matrix. This involvement typically affects a couple to three glomerular lobules, leading to subsequent collapse and features indicative of lobular sclerosis. Additionally, a prominent chronic inflammatory interstitial infiltrate and interstitial fibrosis are observed.

20.17 Focal segmental glomerulosclerosis - Jones methenamine silver staining

The slide shows renal corpuscles with heterogeneous aspects: some are completely sclerosed, while others show an apparently intact glomerular tuft. Some demonstrate slight hypercellularity of endothelial cells, while others exhibit mesangial hypercellularity accompanied by increased mesangial matrix. This involvement typically affects a couple to three glomerular lobules, leading to subsequent

collapse and features indicative of lobular sclerosis. Additionally, a prominent chronic inflammatory interstitial infiltrate and interstitial fibrosis are observed.

20.18 Focal segmental glomerulosclerosis - Congo red staining

The slide shows renal corpuscles with heterogeneous aspects: some are completely sclerosed, while others show an apparently intact glomerular tuft. Some demonstrate slight hypercellularity of endothelial cells, while others exhibit mesangial hypercellularity accompanied by increased mesangial matrix. This involvement typically affects a couple to three glomerular lobules, leading to subsequent collapse and features indicative of lobular sclerosis. Additionally, a prominent chronic inflammatory interstitial infiltrate and interstitial fibrosis are observed.