

1st class: Cell injury and cell death

1. Infarct of the kidney

The infarct consists of coagulative necrosis retaining shadow remnants of previously present vital structures – namely glomeruli and tubuli. The margins of the sample contain vital tissue separated from the necrosis by so-called demarcation cuff composed of mixed inflammatory infiltrate rich in neutrophils and hyperemia.

2. Caseous necrosis

This section of the lung shows irregular foci of homogenous eosinophilic necrosis with dispersed basophilic caryorrhectic material surrounded by a cuff of granulomatous tissue composed of epithelioid cells and multinucleated Langhans cells. These cells are of giant size and possess multiple nuclei in a horseshoe-like arrangement. This is a typical case of tuberculosis.

3. Hemorrhagic necrosis of the intestine

The slide shows a cut section of the small intestinal wall. The mucosa is largely pervaded by erythrocytes and focally frankly necrotic leaving only shadowy outlines of villi with no epithelium on the surface. The submucosa shows marked edema and copious hemorrhages. Vessels are dilated and engorged with blood, surrounded by leukocytic exudate. The subserosal connective tissue shows hemorrhage and edema, and it also contains inflammatory cells.

4. Encephalomalacia

Foci of brain tissue in this specimen underwent liquefactive necrosis which is best seen as a localized collection of so-called "granular" cells (macrophages with abundant pale foamy cytoplasm containing lipids).

2nd class: Cellular adaptations, intracellular accumulations, pigments, crystals calcification

1. Liver steatosis

The original tissue structure is well preserved. The steatotic (fatty) hepatocytes appear lighter because they contain lipid vacuoles in their cytoplasm which stand out as smaller or larger "empty" cavities. This is so because lipids are dissoluted during routine tissue processing and thus lipid droplets are represented by unstained areas.

2. Cholesterolosis of the gallbladder

You can see pale foci in the distended mucosal folds of the gallbladder. These foci are composed of foamy cells representing histiocytes filled with cholesterol.

3. Pulmonary anthracosis

Even grossly you can see the foci of accumulation of coal dust as dark spots in the specimen. The black pigment is deposited mainly in the interstitium along bronchi and vessels. Some alveoli contain alveolar macrophages with the pigment in the cytoplasm.

4. Pulmonary hemosiderosis

This is an example of accumulation of a hematogenous pigment in the lung. The pigment can be seen as red-brown granules in the cytoplasm of alveolar macrophages (called siderophages in this setting). The most common cause of pulmonary hemosiderosis is chronic venostasis due to left heart failure.

5. Metastatic calcification of lung

This specimen shows areas of thickening of alveolar septae. On closer inspection, deposits of bluish-gray calcium salts can be seen in the interstitium and blood vessels of the septae. Focally, there is homogenous eosinophilic edematous fluid present in the alveoli.

3rd class: Inflammation

1. Suppurative bronchopneumonia

Majority of the alveolar spaces in this specimen of pulmonary parenchyma are filled with inflammatory exudate composed mostly of neutrophils and a few macrophages. There is inflammatory edema in some alveolar spaces. Interalveolar septae reveal numerous congested alveolar capillaries. Note the leukocytic exudate in small bronchioli.

2. Acute appendicitis

You can see transverse section(s) of the appendix. Acute appendicitis is characterized by filling of the appendiceal lumen with purulent exudate which even fills the mucosal ulcers. Furthermore, diffuse purulent (i. e. phlegmonous) infiltration is apparent in the deeper layers of the wall (submucosa and muscularis propria). Therefore, acute appendicitis is also regarded as "ulcerophlegmonous".

3. Pseudomembranous colitis

This slide demonstrates a transverse section through the wall of large intestine with mucosa showing signs of focal necrosis (shadowy outlines of crypts losing their lining which may impart the morphology of so-called "signet-ring" cells) covered with fibrinopurulent exudate with necrotic debris (= pseudomembranes). The submucosal connective tissue exhibits sparse mixed inflammatory infiltration and edema.

4. Chronic gastritis

There is a dense chronic lymphoplasmocellular infiltrate in the gastric mucosa. You can also see several lymphoid follicles in the mucosa. As a consequence of the chronic inflammation, mucosal atrophy (separation of glandular structures) and complete intestinal metaplasia (presence of intestinal-like glands containing enterocytes, goblet cells and Paneth cells in the anatomically defined gastric mucosa) may occur.

5. Sarcoidosis

This section shows a sample of the lung or peribronchial lymph node which contains dispersed irregular eosinophilic nodules. Under higher power magnification, these foci can be interpreted as non-caseating granulomas consisting of epithelioid histiocytes and sparse Langhans cells. As the designation "non-caseating" implies, the granulomas of sarcoidosis lack caseous necrosis.

4th class: Disorders of blood flow

1. Pulmonary edema

The lung tissue is almost completely airless. Alveoli are filled with pale eosinophilic (pink) fluid.

2. Chronic venostasis of the liver

Portal tracts are devoid of remarkable changes but lobules show signs of chronic congestion, namely centrilobular atrophy of liver cell plates and dilation of sinusoids filled with erythrocytes. Some of these dilated sinusoids form so-called tracts of congestion in zone 3 of liver acini, occasionally connecting neighbouring central veins. Focally there are even necroses composed of groups of small eosinophilic anuclear hepatocytes surrounded by neutrophils in the centrilobular zone.

3. Recent thromboembolus

In this section of lung parenchyma there are alveoli, bronchi, and two larger branches of pulmonary artery with lumen narrowed by embolus composed mainly of eosinophilic fibrin and in minor part of all types of blood cells.

4. Organized thromboembolus

In the centre of the sample there is a transverse section of a branch of pulmonary artery narrowed by newly formed fibrous tissue consisting of fibrocytes, scanty capillaries and abundant weakly eosinophilic extracellular material.

5. Pulmonary infarct

In this section of pulmonary tissue, there is a wedge shaped hemorrhagic infarct with its base at the pleural surface and the apex pointing toward the hilus of the lung. Histologically, it is characterized by effacement of alveolar architecture of the lung, i. e. the whole focus is hypereosinophilic, the oulines of interalveolar septae are blurred, and (except for nuclei of leukocytes) no basophilic nuclei are present in the alveolar walls. Furthermore, alveoli are filled with red blood cells. In alveoli outside the infarct, alveolar macrophages with phagocytosed hemosiderin (siderophages) can be found.

5th class: Etiological pathology

1. Pulmonary silicosis

There are several quite well circumscribed eosinophilic nodules of various size composed of hyalinized connective tissue in pulmonary parenchyma. These nodules are surrounded by deposits of anthracotic pigment and chronic inflammatory infiltrate. In higher magnification you can discern the roughly fibrillar nature of the nodules, which are descriptively called anthracohyaline nodules. In H&E stained sections the silica crystals are not seen. They can be visible in polarized light, thus confirming the diagnosis of silicotic nodule.

2. Candidiasis

This specimen represents transverse section of esophageal or gastric wall. There is a mucosal erosion filled with fibrinopurulent exudate, necrotic debris, and filamentous pseudohyphae of Candida albicans which are better seen in PAS-stained sections (bright violet).

3. Aspergillosis

In this pulmonary specimen there is a sharply delineated focus of necrotizing pneumonia combining features of inflammation and hemorrhagic necrosis adjacent to a vessel filled with a thrombus containing hyphae of Aspergillus. The mold is barely visible in H&E stained sections, but can be readily identified in a section stained with silver impregnation technique according to Howard-Tseng (HT).

4. Tularemia

The slide contains a lymph node possessing voluminous and well circumscribed granulomas resembling pieces of puzzle in low magnification. In higher magnification you can distinguish central necrosis and peripheral pale cuff of epithelioid macrophages. Multinucleated giant cells are present only in low numbers. Descriptively the lesion should be called granulomatous necrotizing lymphadenitis.

5. Enterobiosis of appendix

The appendiceal lumen contains not only faeces, but also pieces of a pinworm, which can be recognized thanks to the presence of internal organs, mainly digestive tract, less commonly even gonads.

6th class: Immunopathology

1. Amyloidosis

Amyloid in this specimen can be found in spaces between liver cell plates. It is a structureless homogenous eosinophilic material. Hepatocytes underwent severe atrophy.

2. Churg-Strauss syndrome

In this slide, there is a section of the wall of small intestine with extensive ulcer. Beneath the ulcerated mucosa, the wall is infiltrated by mixed inflammatory infiltrate rich in eosinophils. Furthermore, small epithelioid granulomas with several multinucleated giant cells, and small vessels showing necrotizing vasculitis can be found in the inflamed intestinal wall.

3. Autoimunne thyroiditis

The thyroid gland is heavily infiltrated by lymphocytes and plasma cells. In some areas, lymphocytes form lymphoid follicles with germinal centers. Focally there are solid nests and microfollicles containing small amount of dense colloid and composed of cells possessing abundant eosinophilic finely granular cytoplasm. The cells containing these granules (multiplied megamitochondria) are called oncocytes and they originate from thyrocytes during chronic autoimunne thyroiditis.

4. LESA (lymphoepithelial sialadenitis)

Salivary gland tissue shows heavy lymphocytic and plasma cell infiltration which causes focal complete destruction of original structure of the gland. Within the dense inflammatory infiltrate, hyperplastic epimyoepithelial islands can be identified. Their presence is why this condition was previously called myoepithelial sialadenitis (MESA).

7th class: Epithelial tumors

1. <u>HSIL</u>

At one edge of the specimen you can see endocervical glandular columnar epithelium, at the other edge there is a non-keratinizing squamous epithelium. The central part of the specimen is covered with dysplastic squamous epithelium which, however, does not show invasion into the stroma. The dysplastic epithelium shows loss of stratification, and at higher magnification nuclear polymorphy and high mitotic activity are apparent. The changes are seen in almost whole thickness of the epithelium which classifies the dysplasia as CIN 3 (cervical intraepithelial neoplasia) or HSIL (high-grade squamous intraepithelial lesion).

2. Squamous cell carcinoma of the esophagus

The esophageal mucosa at the edge of the sample is covered with normal squamous epithelium (regular stratification and inconspicuous regular nuclei with several mitoses in the basal zone). This epithelium is directly adjacent to the dysplastic one which loses its regular architecture, is composed of irregular cells with polymorphic and hyperchromatic nuclei containing mitoses even beyond the presumed basal layer. Furthermore, there are foci of dysplastic epithelium in deeper layers of the wall which is due to the invasive growth of the tumor.

3. Adenoma of the colon

One piece of tissue represents a normal wall of the large intestine. The second piece should be continuous with the first one, but due to oblique section may look separated. The second piece consists of a stalk and head of a polypous adenoma. While the stalk is covered with normal mucosa consisting of regularly arranged crypts lined with goblet cells and colonocytes with mature cytoplasm and a regular nucleus located at the base of the cell, the dysplastic mucosa of the head of the polyp contains irregularly arranged crypts lined with less mature cells containing stratified, enlarged, elongated and hyperchromatic nuclei.

4. Adenocarcinoma of the colon

As in the previous slide, you can see transition of a normal mucosa to the dysplastic one (atypical crypt architecture and atypical cytology of the lining cells). However, there is a neoplastic infiltration beyond basal membrane in this case. Therefore, it is an invasive tumor infiltrating even the muscularis propria.

5. Transitional cell papillocarcinoma of the urinary bladder

There is a specimen of bladder wall with adjacent prostate in the slide. One edge of the specimen is covered with normal transitional cell epithelium. The rest of the epithelium is transformed into a papillary tumor whose fibrovascular papillae are covered with increased number of rows of nuclei of transitional cells possessing polymorphic nuclei, nuclear hyperchromasia and infrequent mitoses.

8th class: Mesenchymal and other tumors

1. <u>Lipoma</u>

The specimen contains only a part of the tumor. It is well circumscribed and enveloped by a rim of fibrous capsule. The tumor itself is composed of mature adipocytes containing large fatty vacuole and a tiny nucleus devoid of atypia.

2. Hibernoma

This slide also contains only a part of a larger tumor. Beneath the capsule, there are not only common adipocytes, but also groups of fat cells containing many tiny lipid vacuoles and a small nucleus without atypia.

3. Chondrohamartoma

This specimen shows a circumscribed tumor of the lung composed mostly of hyaline cartilage. The cartilage is divided into lobules by septae composed of adipous and fibrous tissue. Slits lined by respiratory epithelium may also be seen between lobules of cartilage.

4. Chondrosarcoma

You can see an irregularly shaped cartilaginous tumor expansively growing into the surrounding soft tissue. It is a well differentiated tumor, which manifests its malignant potential by the presence of irregular arrangement of groups of lacunae, presence of more than one cell in some of the lacunae, and nuclear enlargement and hyperchromasia. The possibility of chondroplastic osteosarcoma should be excluded by ruling out presence of "malignant" osteoid.

5. Cavernous hemangioma

The cutaneous surface is focally elevated above the surrounding niveau due to focal accumulation of large vascular spaces filled with erythrocytes. There is an ulceration above this tumor caught in one section.

6. Angiosarcoma

In this cutaneous excision biopsy there is an ill-defined lesion obviously darker (more basophilic) than the surrounding dermis and infiltrating approximately half of the specimen beneath the intact epidermis. Higher magnification shows that the tumor contains slit-like spaces, some of them containing red blood cells, which proves the vascular origin of the neoplasm. Prominent dark irregular nuclei of endothelial cells protruding into the lumen (in comparison with the previous slide) are a sign of malignancy, which confirms the diagnosis of angiosarcoma.

9th class: Pathology of reproduction

1. Abortion

The specimen is composed of material obtained by curretage of uterine cavity. It consists of maternal parts represented mainly by decidua, and of fetal parts, mostly chorionic villi covered by trophoblast. The material comes from approximately 6th-7th gestational week.

2. Tubal pregnancy

The cross section of fallopian tube shows dilation of lumen and focal hemorrhage in the wall. The lumen contains blood clots and chorionic villi.

3. Partial hydatidiform mole (molar pregnancy)

This material comes from the curretage of uterus in approximately 9th week of gestation. It contains large parts of decidua, and enlarged swollen chorionic villi with central pseudocystic "cistern" formations. Their outline is scalloped and may form deep invaginations. Trophoblastic proliferation is seen on the surface of the villi. Other villi look normal and are devoid of the changes described above.

4. Chorangioma

In this specimen of placenta (3rd trimester) you can see normal chorionic villi with maternal blood within the intervillous spaces. However, even in low magnification, a well circumscribed solid eosinophilic nodule which is seen beneath the fetal surface. The nodule represents an enlarged chorionic villus distended with numerous capillaries with erytrocytes. The lumens of these capillaries can be seen only in high power magnification.

5. Hyaline membrane disease

This slide demonstrates a lung of a preterm infant with infant respiratory distress syndrome (IRDS). Terminal airways are lined by amorphous eosinophilic material (hyaline membranes) composed of necrotic debris and proteinaceous material mostly composed of fibrin.

10th class: Cardiovascular system

1. Atherosclerosis

The section contains atheroma of the aorta which is mostly composed of homogenous to granular eosinophilic substance with dispersed empty clefts representing dissoluted cholesterol crystals. Besides that you may see thickening of intima by hyalinized collagenous tissue with focal calcifications.

2. Myocardial infarct

In the slide there is myocardium and subepicardial fat. Foci of accumulated polynuclear leucocytes are dispersed within myocardium. These leucocytes surround necrotic cardiomyocytes which are thinner then the normal ones, wavy, possess hypereosinophilic cytoplasm, and lack nuclei.

3. Myofibrosis

Myocardium contains scarcely scattered tiny foci of hypocellular weakly eosinophilic collagenous tissue (disseminated or dispersed myofibrosis/myofibroses) which may focally coalesce to form a smaller post-infarction scar. Neighbouring cardiomyocytes possess irregular and hyperchromatic nuclei with coarser chromatin which is the most reliable histological sign of myocardial hypertrophy.

4. Senile cardiac amyloid

Superficially, this sample resembles disseminated myofibrosis due to chronic ischaemic heart disease. However, under low magnification you can see the rounded configuration of regularly distributed lightly eosinophilic foci (in contrast to myofibrosis which is formed by irregularly distributed stellate scars). Furthermore, under high magnification you can appreciate the acellular quality of amyloid (in contrast to the scars of myofibrosis which contain fibrocytes and capillaries).

5. Fibrinopurulent pericarditis

The section consists of a thin layer of right ventricle myocardium and adjacent epicardium which is thickened due to inflammatory edema and contains mixed inflammatory infiltrate. Furthermore, there is a thick layer of fibrinopurulent exudate on the surface of epicardium. The exudate is composed mainly of amorphous eosinophilic fibrin and foci of accumulated neutrophils.

11th class: Hematopathology

1. <u>NHL – follicular lymphoma</u>

Lymph node structure is greatly effaced with a multinodular infiltrate composed of germinal center cells lacking mitoses. Fuzzy edge of neoplastic nodules blurs mantle zone which becomes inapparent. As opposed to the follicular hyperplasia, there are no tingible body macrophages in the neoplastic nodules.

2. <u>NHL – SLL/CLL</u>

The whole slide is diffusely infiltrated by a monotonous population of small round lymphocytes with clumped chromatin, inconspicuous nucleoli, barely visible cytoplasm, and scanty mitotic activity. Although the finding resembles normal lymphoid tissue, the tumor lacks any follicles, and the neoplastic lymphocytes are larger than normal ones, and their nuclei are less regular.

3. NHL - DLBCL

The section is completely infiltrated by lymphoid elements. However, in comparison with the two previous slides the neoplastic cells are much larger, almost of epithelioid appearance, with highly polymorphic nuclei, some of them having bizarre shapes, many of the nuclei being vesicular, with conspicuous nucleoli. Furthermore, there are numerous mitoses in the tumor.

4. HD-NS

This type of Hodgkin's lymphoma is characterized by broad collagen bands separating the lymphoid tissue in well-defined nodules composed of a background of reactive inflammatory cells (mature lymphocytes, eosinophils, plasma cells and histiocytes) and proper neoplastic cells – RS cells and Hodgkin's cells, including lacunar variants. However, the neoplastic cells are scarce.

5. Plasma cell myeloma

The slide contains bone marrow composed of fat tissue and hematopoietic elements. High magnification reveals that cellular regions of bone marrow are not formed by usual trilinear hematopoesis, but are infiltrated with monoclonal population of plasma cells.

6. Eosinophilic granuloma

Histologically, it is characterized by infiltration by cells with inconspicuous faintly eosinophilic cytoplasm and characteristic nuclei that are folded or grooved resembling a coffee bean. Furthermore, this infiltration is accompanied by an admixture of lymphocytes, neutrophils, and quite eye-catching clusters of eosinophils.

12th class: Head & Neck

1. Pleomorphic adenoma

The tumor consists of an epithelial component forming nests, tubules and strands of epithelial cells, and a "mesenchymal component", which focally shows myxoid (composed of spindled, stellate or plasmacytoid myoepithelial cells dispersed in loose myxoid stroma) and focally chondroid (composed of nodules of cartilage) differentiation. There is also a thin rim of normal glandular tissue at the periphery of the sample.

2. Warthin's tumor

This is a cystic tumor of the parotid gland. It consists of a papillary epithelial lining with oncocytic transformation of luminal columnar cells (cells with abundant eosinophilic granular cytoplasm), inconspicuous cuboid to flattened basal cells, and a stroma rich in lymphoid tissue containing lymphoid follicles.

3. Adenoid cystic carcinoma

In the slide there is an infiltrative cancer displaying a so-called "cylindromatous pattern". The neoplastic cells produce abundant extracellular matrix composed mainly of the basement membrane constituents. This material surrounds epithelial nodules and fills the cavities ("cylinders") inside the nodules.

4. Mucocele

Beneath the squamous epithelium of the oral mucosa there is fibrous tissue, striated muscle and a mixed salivary gland containing a cavity filled with foamy macrophages ingesting mucus. These macrophages (muciphages) also line the wall of the cavity.

5. Branchial (cleft) cyst

Although this material resembles a lymph node under low magnification, in fact it is a. cavity filled with cellular debris containing cholesterol clefts, lined with a squamous epithelium and surrounded by lymphoid tissue. Histologically, it is a lymphoepithelial cyst. It is presumed to originate from branchial cleft remnants.

13th class: Respiratory system

1. Lobar pneumonia

This type of pulmonary inflammation shows diffuse distribution throughout the lobe. All alveoli are filled with fibrinous to fibrino-purulent exudate, grossly viewed as "gray hepatisation". Some alveoli show early stage of exudate organization, i. e. its replacement by granulation tissue rich in fibroblasts.

2. Pulmonary squamous cell carcinoma

In the lung there is a focus of islands of squamous epithelium with cytologic and architectural neoplastic atypia. Squamous epithelium is characterized by polygonal cell outline, lack of mucus production, presence of intercellular bridges and keratinization either in the form of keratin pearls or voluminous polyedric cells with strikingly eosinophilic cytoplasm. In the stroma there is a dense inflammatory, mainly lymphocytic, infiltration. Focally you can see foreign body type giant cells, neoplastic islands contain focal necroses.

3. Pulmonary adenocarcinoma

The sample is widely infiltrated by adenocarcinoma, i. e. a neoplasm forming glandular lumina and producing less or more mucus. However, focally the tumor grows in a solid fashion thus creating possible diagnostic confusion with squamous cell carcinoma.

4. Pulmonary carcinoid

Carcinoid is a neoplastic proliferation of neuroendocrine cells, which are quite small, uniform, and posses moderate amounts of weakly eosinophilic cytoplasm. Their nuclei are quite uniform, rounded, with mildly granular "salt and pepper" chromatin. The cells are arranged in larger sheets, ribbons and trabeculae. Focally you can see separation of neoplastic trabeculae from fibrovascular stromal cores due to fixation artifact, which may give rise to an impression of forming glandular lumina leading to possible confusion with adenocarcinoma.

5. Small cell carcinoma of the lung

In the periphery of the slide you can find normal pulmonary tissue, closer to the center of the specimen there is a larger bronchus, which is surrounded by ill-defined infiltration by individually growing dark and small cells, virtually composed only of nuclei and lacking cytoplasm. This makes the neoplastic cells reminiscent of lymphocytes. However, if you use high magnification and compare the neoplastic cells with real lymphocytes, you can see that the neoplastic cells are several times larger. Their nuclei are hyperchromatic, pleomorphic, with coarse chromatin.

14th class: Gastrointestinal tract

1. Gastric peptic ulcer

The wall of the stomach in this slide is partly covered by inflamed antral mucosa which ends abruptly and is replaced by an ulcer extending to submucosa. The surface of the ulcer is covered with fibrinopurulent exudate and necrotic debris. Beneath this layer there is inflammatory granulation tissue, and finally there is fibrosis in the deepest layer of the ulcer. The immediately adjacent mucosa shows reactive architectural and cytologic atypia.

2. Intestinal type adenocarcinoma of the stomach

An ulcer can be seen even in this slide. But in this case you can see neoplastic irregular tubular glands infiltrating fibrous stroma at the base of the ulcer. Surrounding mucosa shows chronic gastritis, atrophy and intestinal metaplasia.

3. Diffuse type adenocarcinoma of the stomach

In the submucosa of this stomach there is a nodule consisting of dyscohesive "signet ring cells", i. e. round cells with voluminous mucin-rich cytoplasm and a nucles pushed aside to the cell membrane. Under higher magnification you can find these cells sparsely infiltrating mucosa adjacent to one edge of the sample. In contrast to the previous case, there is no atrophy and intestinal metaplasia in the adjacent non-neoplastic mucosa.

4. <u>Neuroendocrine tumor of appendix</u>

At a first sight it is not difficult to recognize features of acute ulcerophlegmonous appendicitis, however you should keep in mind that our body may suffer from more than one disease. Thus, you should check the whole slide for possible presence of "something more". In this slide there should be ale least one section of appendiceal wall infiltrated by pale nodules composed of quite bland-looking cells with amphophilic cytoplasm and monomorphic rounded nuclei with finely granular "salt and pepper" chromatin. This type of tumor you were already shown in the Respiratory system practical, under its traditional name "carcinoid".

5. <u>GIST</u>

This slide contains a mural neoplasm of the wall of small intestine covered with intact mucosa and submucosa. The tumor arises from muscularis propria and it protrudes beneath serosa. The neoplasm consists of population od spindled cells with weakly eosinophilic to amphophilic cytoplasm. This type of tumor is the most frequent mesenchymal tumor of the digestive tract and is called "gastrointestinal stromal tumor".

15th class: Hepatobiliopancreatic tract

1. <u>Liver cirrhosis</u>

In the slide there is a nodular rearrangement of a normal lobular architecture of the liver. The parenchymal nodules are surrounded with fibrous septae containing ductular proliferation and mild focal chronic inflammatory infiltrate. The nodules consist of two cells thick liver cell plates. The normal portal to centrolobular stratification is lost in the nodules of cirrhosis.

2. Hepatocellular carcinoma of the liver

The malignant tumor arising from hepatocytes is distinguishable from non-neoplastic liver tissue due to architectural atypia (at least three cells thick liver trabeculae, acinar structures) and cytological atypia (anisomorphic and vesicular nuclei). The fibrous capsule separates the tumor from the adjacent non-neoplastic liver tissue containing chronic inflammatory infiltration and cirrhosis.

3. Chronic cholecystitis

The most striking feature of chronic cholecystitis is fibrous thickening of the wall of the gallbladder. The fibrosis is present in all layers of the wall but the most severe changes are present in the subserosa. Furthermore, you can see atrophy of mucosal folds and mild chronic inflammatory infiltration. Unfortunately, epithelium is almost completely detached, better seen in mucosal infoldings called Aschoff-Rokitansky sinuses which focally display pseudopyloric metaplasia.

4. Chronic pancreatitis

The glandular tissue is partly replaced by fibrous tissue containing focal chronic inflammatory infiltration. In the center of the slide there is a small postnecrotic pseudocyst with wall consisting of granulation tissue containing numerous foamy macrophages. The cavity of the pseudocyst contains necrotic debris. Some pancreatic ducts show features of reactive proliferation. Focal calcifications are a sign of alcoholic origin.

5. Pancreatic adenocarcinoma

The specimen is partially composed of residual normal glandular pancreatic tissue with preserved lobules of acini. However, some lobules underwent atrophy and were replaced by fibrous tissue containing dysplastic ducts. In the neighbourhood there is an infiltration by irregular neoplastic glands lined with highly atypical cells. Some of these glands are composed only of clusters of several cells devoid of identifiable lumens.

16th class: Urinary system

1. <u>Hydronephrosis</u>

The first diagnostic sign is the fact that you can see the whole thickness of renal parenchyma in the slide. Furthermore, there is no papilla protruding into the calyx due to its flattening resulting from pressure atrophy. Wide empty space beneath the atrophic medulla presents dilated calyx. Renal parenchyma shows tubular atrophy, fibrosis and chronic inflammatory infiltration of interstitium.

2. Purulent pyelonephritis

Among characteristic renal structures (glomeruli and tubules) you can see purulent inflammatory exudate focally even forming circumscribed cavities filled with pus (abscesses). Neutrophils do not infiltrate only the interstitium but also some tubules. Therefore, this is a case of purulent tubulointerstitial nephritis. This mainly evolves through ascendent pathway and thus it should also present inflammation of the renal pelvis (pyelonephritis).

3. Clear cell renal carcinoma

Normal parenchyma of the kidney is sharply separated from a rounded tumor consisting of tubules, alveoli and solid trabeculae of polygonal cells with clear cytoplasm. There is a rich vascular network among the neoplastic cells. The water clear appearance of cytoplasm is caused by dissolution of intracellular fat and glycogen during tissue processing.

4. Papillary renal cell carcinoma

This tumor of the kidney is composed of papillae covered with neoplastic columnar epithelial cells possessing eosinophilic cytoplasm. Some slides may contain occasional macrophages and/or calcifications.

5. Renal angiomyolipoma

This specimen demonstrates a distinctive benign mesenchymal tumor composed of three different tissue components: mature adipose tissue showing a slight variation in cellularity, thick-walled blood vessels, and irregular bundles of smooth muscle cells that focally may be seen to merge with the vessel wall.

17th class: Male genital system

1. Prostatic hyperplasia

Histological picture of prostate is characteristic because of presence of fibromuscular stroma and serrated glands lined with columnar epithelium. Benign nature of the prostatic enlargement (hyperplasia) is morphologically verified by bland cytology of glandular cells and by the presence of a layer of inconspicious basal cells adjacent to the layer of glandular cells.

2. Prostatic adenocarcinoma

This slide contains several lobules of benign prostatic glands surrounded with fibromuscular stroma. However, major part of the slide is infiltrated by small neoplastic nonserrated glands displaying cytologic atypia of glandular epithelium (high nuclear/cytoplasmic ratio, anisokaryosis, nuclear hyperchromasia, conspicious nucleoli) and absent basal cell layer (i. e. the glands are lined by only one row of nuclei).

3. Purulent orchiepididymitis

The slide consists mostly of a testis with inflammatory infiltration of stroma and tubules, which is mainly lymphoplasmocellular in the periphery, but becomes more rich in neutrophils towards the center. In the center, there is an abscess containing necrosis and purulent exudate.

4. Seminoma of testis

Epidydimis, a part of testis, and a tumor composed of nodules separated by incomplete fibrous septae are shown in the slide. The tumor is characterized by sheets of large polygonal neoplastic cells with water-clear cytoplasm with distinct cell borders and only mildly atypical nuclei. Typically, the interstitial tissue of seminoma contains foci of lymphocytic infiltration.

5. Mixed germ cell tumor of testis

There is a mixture of three merging components in this testicular tumor. First, there is a seminoma of similar appearance as in the previous slide present in the specimen. Further, you can find foci of yolk sac tumor, best recognizable as small cystic structures lined by cells with incospicuous cytoplasm or forming glomeruloid structures. The third component is embryonal carcinoma composed of undifferentiated carcinomatous tissue possessing dark and irregular nuclei, focally forming adenocarcinomatous tubules.

18th class: Female genital system

1. <u>LSIL</u>

In the slide there is endocervix with superficial squamous metaplasia of the mucosa. The squamous cells show koilocytosis (enlarged hyperchromatic and irregular nuclei surrounded by perinuclear vacuole) in superficial layers and dysplastic changes with loss of stratification in the basal third of epithelium. The fact that the dysplasia is restricted to the basal third of epithelial thicknes defines the intraepithelial lesion as CIN I (cervical intraepithelial neoplasia grade I), which is a part of spectrum of LSIL (low grade squamous intraepithelial lesion).

2. Squamous cell carcinoma of the cervix

One edge of the sample contains normal ectocervical mucosa, but the rest of the tissue is infiltrated by moderately differentiated squamous cell carcinoma invading deep into the fibromuscular stroma of the cervix. The islands of neoplastic cells with polygonal shape and abundant eosinophilic cytoplasm surround residual non-neoplastic endocervical glands lined with columnar mucinous epithelium.

3. Ovarian teratoma

The slide contains a part of a cyst wall lined with keratinizing squamous epithelium. Beneath the epithelium there are sebaceous glands, hair follicles and sweat glands. But, in contrast to a skin sample you can also find neuroglial tissue and focal accumulation of mature ganglion cells in nodular arrangement resembling a ganglion of autonomic nervous system. Although you may be unable to find structures that morphologically define ovary, this weird mixture of tissues is characteristic for the diagnosis of mature cystic teratoma. This type of tumor may also contain cartilage, bone, teeth, tissues of respiratory and digestive systems and others.

4. Ovarian serous adenocarcinoma

Residual ovarian cortex with several corpora albicantia helps to identify the tissue of origin in this case. On the ovarian surface, but focally also in the ovarian stroma you may find neoplastic cells with large polymorphic nuclei and voluminous eosinophilic cytoplasm forming papillary structures. The diagnosis of this type of tumor may be further confirmed by occasional finding of psammoma bodies.

5. Ovarian mucinous cystadenoma

The tumor takes the form of a multilocular cyst whose spaces are lined by a single layer of benign columnar mucin-producing epithelium (nuclei at the base, pale cytoplasm). The cystic spaces are filled with a mucous fluid. Normal ovarian tissue is represented by presence of the strikingly "blue granular" ovarian cortex.

19th class: Mammary gland

1. Fibrocystic disease

In this specimen, the ducts and acini of the mammary gland are focally replaced by fibrous tissue. Residual lobules show atrophic and hyperplastic changes. Some ducts are dilated with formation of cysts. Rare foci show apocrine metaplasia of epithelium.

2. Mammary fibroadenoma

Fibroadenoma is a benign biphasic tumor composed of epithelial and mesenchymal components. The epithelial component is composed of slit-like spaces lined by ductal epithelium. The mesenchymal component of the neoplasm consists of hypocellular fibrous nodules compressing the ducts. Neither the epithelial nor mesenchymal components exhibit significant mitotic activity or nuclear polymorphism. The margin of the nodule is well demarcated. Note the nonneoplastic mammary gland tissue at the periphery of the specimen.

3. Mammary invasive ductal carcinoma

Almost the whole slide is infiltrated by more or less luminized neoplastic tubules growing in desmoplastic stroma. Even among these neoplastic glands there are some entrapped benign ducts of the mammary gland, these being much more common in the neighbourhood of the neoplastic nodule. The benign ducts consist of an inner epithelial and outer myoepithelial layers. At the periphery of the specimen some nonneoplastic lobules can be found.

4. Mammary invasive lobular carcinoma

The sample consists of fat and thick irregular band of fibrous tissue containing discohesive inconspicious neoplastic cells with small amount of cytoplasm infiltrating the stroma in an "indian file" pattern.

5. Mammary mucinous carcinoma

This carcinoma is composed mainly of extracellular mucin, within which there are floating tumor cells (isolated or forming small groups). The neoplastic cells are small, with slightly polymorphic basophilic nuclei and eosinophilic cytoplasm. At the margin of the slide, there is a fibroadipose breast tissue with acini and ducts.

20th class: Skin

1. Seborrheic keratosis

This lesion is very common, occurring usually in elderly. Grossly, it is a pigmented verrucous lesion, histologically characterized by squamous cell proliferation with typical presence of many keratin-filled balls (so-called horny cysts or keratin pearls) in the thickened epidermis.

2. Basalioma

The classical variant of basalioma is characterized by infiltration of dermis with nests of neoplastic cells that form a peripheral palisade resembling the basal layer of epidermis. These nests are usually surrounded with an empty cleft which results from arteficial separation of the stroma. There are also some mitoses in the neoplastic cells.

3. Epidermoid cyst

This type of cutaneous keratinous cyst is characterized by epidermal type of keratinization, i. e. presence of granular layer and production of lamellar keratin which usually doesn't undergo keratinization. The majority of these cysts form as a result of progressive ectasia of the infundibulum of the hair follicle.

4. Trichilemmal cyst

The cyst is lined with squamous epithelium lacking granular layer. Spinous layer is immediately adjacent to cornified material filling the cyst. The cornified material is amorphous and contains foci of calcification.

5. Melanocytic nevus

This cutaneous lesion can be seen as an elevation of the skin surface. Dermis beneath this elevated surface contains nests of melanocytes with pale cytoplasm (nevocytes, nevus cells) producing golden-brown endogenous pigment melanin.

6. Malignant melanoma

There are nodules of malignant melanoblasts in the fibrous stroma. The melanoblasts display nuclear atypia and mitoses, and focally they infiltrate the squamous epithelium, even its spinous layer, and, in contrast to regular nests of benign nevi, they form small irregular clusters or even monocellular infiltrates in the epithelium. Focally, there are deposits of melanin in the tumor.

21st class: Bones & Soft tissue

1. Gout

Histological features of chronic gout are represented by gouty tophi. These are deposits of urate crystals surrounded by epithelioid and multinucleated giant histiocytes, granulation tissue and fibrous tissue. Unfortunately, during formaldehyde fixation the majority of the crystals become dissoluted and thus you can see only lightly staining cloudy material in the deposits.

2. Rheumatoid nodules

Rheumatoid nodules represent histological features of an autoimunne systemic disease called rheumatoid arthritis. These nodules consist of brightly pink fibrinoid necrosis of soft tissue surrounded by palisading epithelioid histiocytes.

3. Osteochondroma

This benign tumor is reminiscent of an ordinary small bone covered with articular cartilage. It may be recognized as a tumor (besides the fact that pathologists are not supposed to show normal tissues to you) thanks to the presence of a thin fibrous cap covering the surface of hyaline cartilage which is a proper part of the tumor.

4. Fibrous dysplasia

In the slide, there is a piece of bone focally replaced by abnormal tissue, which consists of cellular fibrous tissue composed of spindled fibroblasts in a moderate amount of collagen. Furthermore, this tissue also contains fine branching, curvilinear trabeculae of woven bone with little evidence of osteoblastic rimming. The lesional bone merges imperceptibly with adjacent normal bone.

5. Giant cell tumor of bone

Nearly the whole sample is composed of the tumor, there are only a few bone trabeculae at the edge of the tissue. The tumor is characterized by eye-catching presence of non-neoplastic osteoclastic multinucleated giant cells, however the cells responsible for this type of tumor are much less prominent spindle and oval mononuclear neoplastic cells.

22nd class: Endocrine system

1. Nodular goiter

There is an almost normally appearing thyroid gland in the slide. However, the tissue is not absolutely regular, but some colloid nodules formed by dilated follicles lined with flattened thyrocytes can be found. These nodules are separated by fibrous septae and areas of follicles of normal size. No neoplastic or inflammatory infiltration can be seen here.

2. Thyroid follicular adenoma

Normal thyroid parenchyma surrounds a rounded nodule circumscribed with a thin fibrous capsule. The nodule displays predominantly microfollicular architecture. Solitary occurrence and encapsulation of the lesion suggests neoplastic nature of the nodule. Absence of nuclear changes typical for papillary carcinoma determines it as a follicular neoplasia, and lack of transcapsular invasion and angioinvasion defines it as a benign tumor – follicular adenoma.

3. Papillary thyroid carcinoma

In this sample of thyroid you can see an ill-defined tumor with focal papillary arrangement. However, nuclear changes in the neoplastic cells – optically clear nuclei, nuclear grooves and pseudoinclusions – are more important for the diagnosis. These changes, which define papillary thyroid carcinoma, are present even in the portion with follicular arrangement of the tumor.

4. Parathyroid adenoma

While normal parathyroid consists of a mixture of main cells, oxyphilic cells and transitory cells arranged in irregular islands separated by fat tissue, this slide contains almost monotonous diffuse population of endocrine cells without any fat tissue. However, you can find a rim of normal parathyroid gland in the periphery, which supports a diagnosis of an adenoma.

5. Parathyroid hyperplasia

This slide also represents a diffuse proliferation of parathyroid cells without any intervening fat tissue. The absence of a normal parathyroid tissue at the edge of the proliferation suggests a possibility of hyperplasia more than a tumor.

23rd class: Nervous system

1. Purulent leptomeningitis

The sample consists of brain tissue and adjacent meninges. In the meninges and between them (in the subarachnoid space), there is a mixed inflammatory infiltrate rich in neutrophils. Sometimes even perivascular spread of the infiltrate into deeper layers of the brain can be found.

2. Astrocytoma

Two parts of this piece of brain can be discerned in the microscope. One part is composed of hypocellular normal white matter, the other part is much more cellular, in this case composed of so-called gemistocytes (a variant of astrocytes possessing abundant cytoplasm). However, it is the increased cellularity and mild nuclear atypia of the neoplastic cells that classify this tumor as diffuse astrocytoma grade 2.

3. Glioblastoma

Almost the whole slide is infiltrated by a necrotic malignant tumor. Three morphological signs occurring in various extent characterize this tumor. First, neoplastic cells are polymorphic and with large hyperchromic irregular nuclei. Second, "geographic" necroses, often surrounded with palisading neoplastic cells can be found. Third, rich abnormal vascularization is typical for this tumor, frequently with proliferation of small vessels forming glomeruloid structures. High variability of the histological picture was mirrored in an older name of this tumor: "multiform glioblastoma".

4. Oligodendroglioma

As in the case of astrocytoma, even here you can find a hypocellular part, composed predomimantly of fibrillar stuctures of white matter, and a hypercellular neoplastic part. The tumor consists of quite uniform cells, frequently with a perinuclear "halo", which imparts a water-clear appearance to the polygonal cytoplasm. This is why the tumor is said to be reminiscent of fried eggs or a pavement made of tiles. Calcospherites are also typically present in this type of tumor.

5. Schwannoma

This slide does not contain (and in fact cannot contain) any diagnostic non-neoplastic tissue. Histologically, the tumor can be recognized if it contains well developed architectural pattern called Antoni type A. This type is cellular, with tightly packed cells typically forming nuclear palisades surrounding pink stripes of cytoplasm (so called Verocay bodies). In Antoni type B the cells are dispersed in rich edematous stroma.